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July 10, 1973

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NEWS & FEATURES From NIH July 10, 1973

Research Advances

Infectious Not Harmless...

UNTREATED CONGENITAL TOXOPLASMOSIS AFFECTS INTELLECTUAL DEVELOPMENT

Untreated subclinical congenital toxoplasmosis may be associated with some degree of intellectual impairment. Treatment of infected infants is justified in the hope of reducing or even avoiding brain damage which might otherwise occur after birth.

These findings result from a study designed to determine the potential hazards of the subclinical form of congenital toxoplasmosis. According to Charles A. Alford, M.D., and colleagues at the University of Alabama School of Medicine, even though subclinical toxoplasmosis does not cause overt mental retardation, the infection cannot be considered harmless.

Similar to congenital rubella, toxoplasmosis acquired in utero can result in premature interruptions of pregnancies, delivery of stillborn infants, or delivery of liveborn infants with severe multiple organ system involvement particularly disasterous to the optic and central nervous systems.

However, severe forms of the disease are relatively scarce. Infection in the newborn infant is usually milder and is often subclinical with respect to distinguishable physical findings.

Dr. Alfrod previously demonstrated that cerebrospinal fluid changes in protein level and cell count are common in so-called subclinical congenital toxoplasmosis. These abnormalities may persist for a number of weeks following delivery and are not accompanied by symptoms of central nervous system damage.

(more)

Toxoplasmosis (Cont'd)

The exact significance of central nervous system changes in the subclinical pattern of the disease in relation to later mental development is presently unknown. To find the significance of these changes, Dr. Alford and colleagues compared the intellectual and social development of eight infected children, ranging in age from 25.1 months to 49.3 months, to that of eight matched control subjects. The controls were matched for chronological age, sex, race, birth weight, age of mother, gestational age, socioeconomic level, and except in three cases, on the marital status of the mother at the time of birth of the child.

The investigators also examined the effects of early treatment.

Use of screening tests in the latter half of the studies permitted early detection of infection in three of the infants in the newborn period. Therapy was instituted shortly after birth and continued for one month. Early nonsymptomatic central nervous system involvement was the most prominent feature of the commonly occurring form of congenital toxoplasmosis in the infected population.

Each child was given a diagnostic test battery and rated by the examiner on a scale for the following behaviors: responsiveness to examiner, responsiveness to mother, cooperation with examiner, reaction to the new and strange, happiness, persistence in goal-directed behavior, activity level, gross muscle coordination, fine muscle coordination, and deviant behaviors.

As a result of this psychological testing, the investigators found that the mean I.Q. (93) of the untreated infected babies was significantly lower than the mean I.Q. (110) of the matched control subjects. In contrast, they

found no difference between the I.Q.'s of the treated infected babies and their control subjects. Except for one nontreated infected child, no clinically apparent behavior deficits were observed between the infected and control subjects.

Although no universal differences were obtained between the groups on the behavior record index, the investigators found several apparent trends in the individual behavior items. For example, they found that the control children had less fearfulness and more acceptance of the testing situation. Also, the infected treated infants showed more persistence in their attending behavior. The nontreated infected babies, however, had poorer gross motor coordination and, to a lesser degree, poorer fine motor coordination.

The investigators also found a negative relationship between I.Q. and chronologic age in both the infected and control children. They report that a lowering of I.Q. with increasing age associated with a relatively reduced verbal ability is not an uncommon finding when testing individuals of low socioeconomic status such as those in this study.

According to Dr. Alford, "The study data indicate that there may be varying degrees of intellectual impairment in children who are born with so-called subclinical toxoplasmosis." The lack of evident intellectual deficits in children who were treated for their infection shortly after delivery is, to Dr. Alford, one of the most intriguing findings of the study. He believes that a significant amount of the brain damage with subclinical congenital toxoplasmosis occurs after delivery and that it may be slowed or ameliorated with adequate therapy.

(more)

Toxoplasmosis (Cont'd)

These conclusions, however, remain tentative until a larger number of infants can be examined over a longer time span. Dr. Alford stresses that because of the high incidence of subclinical congenital toxoplasmosis (1 per 1,000), it is imperative to corroborate these results and determine if a comparable situation exists with other chronic subclinical congenital infections. If this proves to be the case, then the need to perfect the screening methods for detection of specific subclinical infections in the general population will be justified.

Samuel A. Saxon, Ph.D.; Wynelle Knight; David W. Reynolds, M.D.; Sergio Stagno, M.D.; and Dr. Alford reported their findings in *The Journal of Pediatrics*, May 1973. Dr. Alford is a grantee of the National Institute of Child Health and Human Development.

#

Research Advances

PHYSICIAN USES HYPNOSIS TO TREAT CHRONIC PAIN

Hypnosis can be a valuable method for helping patients with acute and chronic pain, according to a Swedish physician who uses the technique.

Basil Finer, M.D., induces hypnosis by helping patients achieve deep muscular and mental relaxation followed by a numbing sensation beginning at the soles of the feet and rising over the whole body.

Dr. Finer, an associate professor of anesthesiology and intensive care at the University of Uppsala, Sweden, discussed his working hypnotherapy at the International Symposium on Pain, held in Seattle on May 25, 1973. The meeting,sponsored by the National Institutes of Health and the University of Washington School of Medicine,was the world's first large-scale conference on the subject of pain. More than 100 speakers attended from countries around the world, including Japan, Italy, England, France, Scotland, Germany, and Sweden.

In some patients, Dr. Finer combines the use of hypnosis with drugs or nerve blocks to treat pain. Other forms of psychotherapy can add to the value of using hypnosis, he reported.

Approximately 90 percent of the population can be hypnotized, Dr. Finer said, especially if subjects are highly motivated. However, hypnosis may not be the proper form of treatment in patients who are not sufficiently susceptible, in persons who may become too dependent on it, or in patients who may withdraw from reality.

In the case of acute pain, hypnosis has been used during major and minor surgery, to relieve an accident victim's pain, and in obstetrics. For patients

(more)

Hypnotherapy (Cont'd)

suffering from chronic pain, hypnosis usually does not bring complete relief, Dr. Finer explained, but may change unbearable suffering to bearable discomfort. Hypnosis may help the patients achieve more spontaneity and combat depression.

Hypnosis may also be used to help the patient overcome the fear of anticipated pain, such as that encountered in general and dental surgery, obstetrics, and in certain postamputation cases.

Dr. Finer emphasized the chronic pain patient's need for social contact and the opportunity to express feelings. By the time such patients seek hypnotherapy, he explained, "they have often been suffering for several years, are desperate, and have been disappointed by previous failures to treat the pain." Because of their chronic suffering, they may be addicted to drugs and/or alcohol. This and various prolonged hospital stays often make chronic pain patients passive and institutionalized, Dr. Finer added. "They have learned during the years that friends, relatives, and hospital staff get tired of hearing of their suffering. These patients feel inferior to others and, at the same time, long to be accepted as they are."

The investigator explained that such feelings breed a strong aggression which seldom finds release. Lack of sleep from pain increases the vicious circle. Unemployment may also be an additional, complicating factor.

"All of these factors contribute to an egocentric, hypochondriacal agitated depression," Dr. Finer said. Participation in creative activities, group discussions, psychodrama, education dramatics and patient clubs often helps patients cope with these problems.

#

Research Advances

NEW PROGRAMS ADVANCED TO EASE CHRONIC PAIN

For individuals suffering chronic pain, the pain becomes a way of life. One of the chief tasks for physicians confronting such long-term pain is to influence the patient back to a normal pattern of behavior.

Many persons who suffer chronic pain achieve various "payoffs" through perpetuation of their pain and thus may be unwilling to have it cease. Richard A. Sternbach, Ph.D., a psychiatrist at the University of California Medical School at San Diego, recently reported on such "pain games."

As examples, Dr. Sternbach cited the "professional" pain patient who, similar to an athlete, receives compensation for his situation in the form of unemployment claims, social security, or legal suits; the "addict," for whom continuing pain is both an official and a self-justification for drug usage; and the "confounder," who feeds his ego by puzzling medical institutions with his pain.

To counter these tendencies among pain patients, Dr. Sternbach suggested that physicians be aware of the potentially manipulative nature of patient-doctor relationships. In addition to the payoff motive, he explained that the over-all motivation in chronic pain patients is often to perpetuate a lifestyle which may include attention and sympathy from others or lack of responsibilities. Physicians must be careful in ascertaining the patient's actual, not just his stated, behavior. They must seek to counteract the pain game by helping the pain patient find realistic and appealing alternatives to a "pain career," Dr. Sternbach said.

(more)

Pain (Cont'd)

If pain is played as a game by some, it is also a "learned" behavior in many persons suffering chronic pain. To free a patient from his learned pain when its actual causes have been removed, it is often necessary to help him "unlearn" it, according to Wilbert E. Fordyce, Ph.D., professor of psychology at the University of Washington Department of Rehabilitation Medicine. Dr. Fordyce, who is supported by the National Institute of Dental Research, has developed an "unlearning" program using operant conditioning techniques.

Dr. Fordyce, along with Dr. Sternbach, reported his findings on May 23, 1973 at the International Pain Symposium near Seattle, Washington. The Symposium was supported by the University of Washington and the National Institutes of Health.

Operant conditioning recognizes the benefits that may accompany chronic pain--rest, attention, time off from work, medication. Dr. Fordyce believes that behavior is influenced by its consequences and that too often family members, hospital staff members, and others reinforce a patient's pain by catering to it.

Instead, Dr. Fordyce said, such reinforcers should be withdrawn and an effort made to increase "well-behavior" (exercise, work, or other activities) Rewards should be used to reinforce this positive behavior. Any gains should be furthered by modifying the patient's environment to reflect and further reinforce his progress. This would include discharge from the hospital, removal of invalid paraphernalia, and increase of responsibilities.

For patients whose pain has been acknowledged and reinforced by regular medication, Dr. Fordyce uses a "pain cocktail"--medication mixed in flavored

(more)

Pain (Cont'd)

syrup to mask the taste. He increases the frequency of medication to anticipate the onset of a pain period and therefore, deprives the patient of his expected pain and breaks the cycle of pain and reward.

Gradually, over a period of six to seven weeks, the medicine in the "pain cocktail" is diminished to zero, though the cocktail is served as usual. In this way the "learned" pain may be phased out of existence, along with a possible drug dependency.

A key element in operant conditioning, Dr. Fordyce said, is honesty between patient and doctor. It is important for the patient to be educated to the nature of his pain and to the steps that will be used to cure him. All steps are disclosed except the reduction of the medication.

#

Photo Feature

CLEMSON UNIVERSITY HOSTS BIOMATERIALS SYMPOSIUM

The need for prosthetics (the replacement of body parts by artificial mechanisms) is quite widespread. It is the rare American who doesn't have at least one dental filling. As many as half the citizens of the U.S. over age 65 are without natural teeth.

Clemson University hosted its Fifth Annual International Biomaterials Symposium in April, co-sponsored by the National Institute of Dental Research, where researchers from 34 states and 11 foreign countries gathered to learn more about prosthetic devices.

The scientists discussed the designing, manufacturing, and the safe implanting of biomaterial devices to restore function destroyed by disease, injury, or birth defect. They studied the mechanical properties of hard tissue, prosthetic design and evaluation, and research indicating that controlled electrical stimulation may be useful in causing regrowth of destroyed cartilage and bone.

The stainless steel hip joint attached to a thigh bone, two artificial ceramic tooth roots that can be implanted into the gums, and an artificial aorta made of Dacron shown above are examples of the kinds of artificial body parts reported on at Clemson University's Fifth Annual International Biomaterials Symposium. (NIH Photo #1078)

The researchers also discussed artificial hip joints and calcification, and deliberated on research

(more)

Biomaterials (Cont'd)

on artificial knee joints, plastic and reconstructive surgery for the facial region, and dental implants.

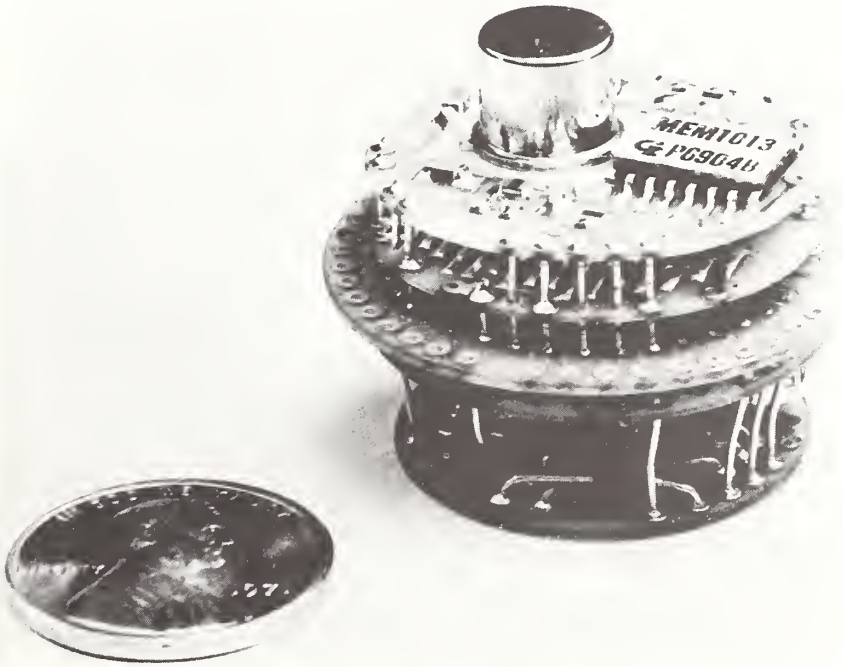
(more)

This artificial total knee joint (left), made of plastic and metallic components, has been successfully transplanted at the George Washington University Medical Center into 35 patients suffering from crippling arthritis. A roentgenogram (below) of the artificial knee three months after implantation into a patient demonstrates its flexibility. The device was the subject of a report at Clemson University's Fifth Annual International Biomaterials Symposium. (NIH Photos #1079, 1080)

Biomaterials (Cont'd)

The use of new biomaterials and prosthetic devices is widespread. For example, there are now more than 95,000 cardiac patients in the United States using pacemakers to activate their hearts. Additionally, more than 10,000 Americans are equipped with artificial heart valves made of stainless steel and dacron mesh. Crippling arthritis disables over 100,000 Americans each year.

The surgeons and engineers who gathered at the Clemson Symposium are collaborating to develop artificial devices made of metallic alloys (stainless steel, vitallium, titanium), plastics (silicone rubber, polyethylene derivatives, Teflon), some ceramics, some forms of pyrolytic carbon (a graphite-like carbon crystal), and other unique substances.



This miniature telemetry device, which can be attached inside an artificial hip joint, sends data about pressure measurements on the hip joint surface to a receiver outside the body. This innovation in artificial organ research was reported on at Clemson University's Fifth Annual International Biomaterials Symposium. (NIH Photo #1081)

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Photo Feature

NIH CLINICAL CENTER MARKS 20TH ANNIVERSARY

The impact of basic science on clinical research and on modern medical practice was discussed on July 6, 1973 at a day-long scientific seminar during the 20th anniversary celebration for the NIH Clinical Center.

The Clinical Center is a 14-story, 516-bed research hospital with twice as much space devoted to laboratories as to patient care areas. It is a modern structure designed to bring scientists working in 1,100 laboratories into close contact with clinicians who are caring for patients.

Many years ago, Public Health Service (PHS) research was largely devoted to investigations conducted at the sites of epidemic outbreaks of infectious diseases. However, as far back as 1911 it was recognized that lack of a clinical facility especially designed for research was hampering the effectiveness of investigations.

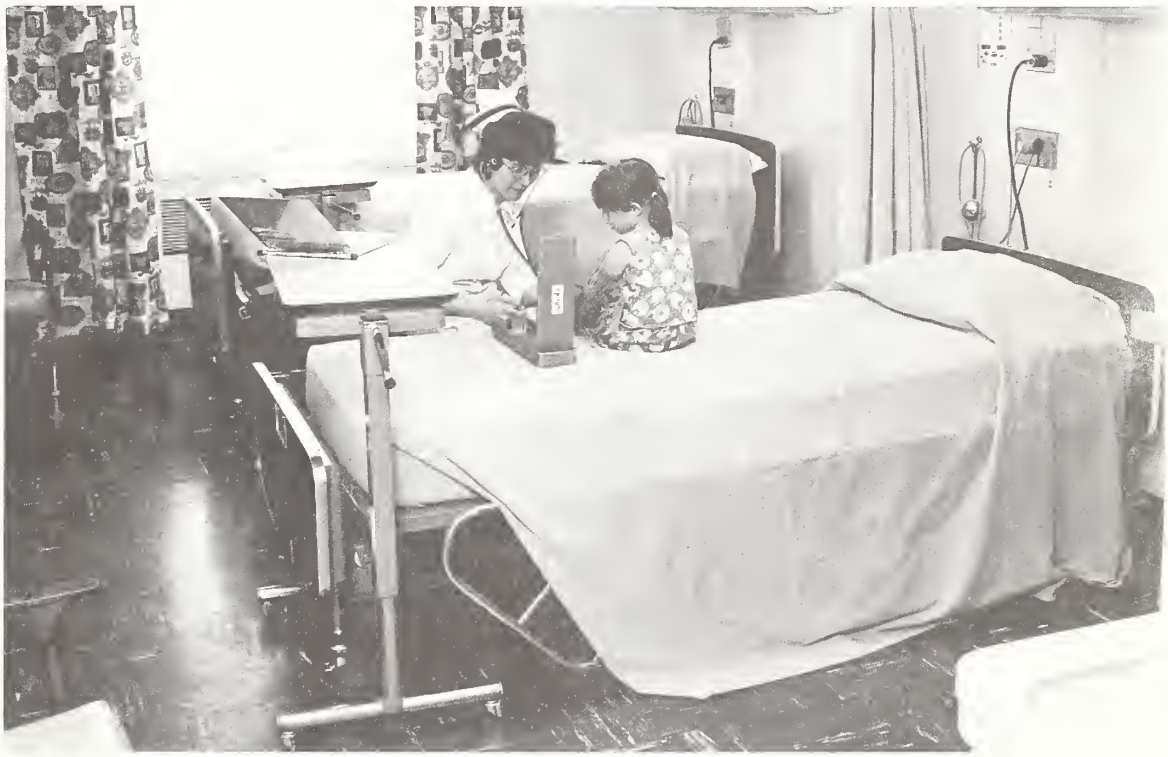
Changing national health patterns led Congress to initiate in 1947, a large expansion of funds for both Federal and non-Federal medical research. The parallel and progressive strengthening of NIH's own research activities in Bethesda made facilities for clinical study essential. Design and construction of the Clinical Center were begun in 1948. The first patients were admitted in 1953.

Authorized by Congress specifically for medical research purposes, the Center does not offer general diagnostic and treatment services in the same sense as do most hospitals. Patients are selected--after referral by their physicians--solely because they have a precise stage of an illness needed in a particular study being conducted by one or more of the Institutes.

(more)

20th Anniversary (Cont'd)

Contrary to the assumption sometimes made by people who think of medical research as being primarily concerned with mysterious and exotic diseases, the illnesses under study at the Clinical Center have always been those which are all too common in people throughout the Nation. Ranging from the common cold to heart disease and cancer, the widespread maladies being investigated reflect a public health mission--to accomplish the most for the greatest number.



The Clinical Center's nurses are specially trained to perform even routine procedures meticulously. Slight variations in vital signs, for instance, could lead to new knowledge about disease. (NIH photo #1082)

(more)

20th Anniversary (Cont'd)

Ongoing research by Blood Bank and other NIH scientists working at the Clinical Center has led to significant advances in control of posttransfusion hepatitis. Their findings provided the foundation for a current FDA ruling that every blood unit be tested for a hepatitis-associated antigen prior to transfusion. The agar plate is used in one of the tests. (NIH Photo #1083)

The Clinical Center's Clinical Pathology Department has been at the forefront of laboratory computerization. Above, a medical technologist reads the results of tests to determine the antibiotic sensitivity of bacteria and then enters data into the computer. The computer will add this information to a report for physicians and store it for future use. (NIH Photo #1084)

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NEWS & FEATURES From NIH July 10, 1973

News Feature

ARTHRITIS, RHEUMATIC DISEASES ARE BIGGEST AMERICAN CRIPPLERS

Eighteen million Americans of all ages are victims of the Nation's number one crippling disorders--arthritis and the rheumatic diseases. Second only to heart disease as the most widespread chronic illnesses in the U.S. today, these ailments cause untold suffering, impose extensive limitations on freedom of movement, and each year cost in excess of $3 1/2 billion in lost wages, medical and disability payments, and taxes lost to the Federal Government.

In Fiscal 1973, the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD), the focal point for conducting and supporting the Government's program of research in arthritis, spent $14.1 million to support research in arthritis. The Department of Health, Education, and Welfare is making disability payments to persons crippled by arthritis at the rate of a billion dollars every ten years.

At a time when every effort is being made to limit Federal expenditures and to eliminate nonproductive programs, it is significant that the budget submitted by the President for 1974 proposes an increase for biomedical research of almost $50 million. The emphasis is on the two major "killers," heart disease and cancer, but all biomedical research will gain from this added support.

A crucial point to remember--one too frequently overlooked in discussions of research in a particular area--is that such investigation is not pursued in a vacuum, in a setting distinct and isolated from other biomedical concerns.

(more)

Arthritis (Cont'd)

On the contrary, biomedical research reflects a continuum of interrelated investigative activities, each contributing to and deriving sustenance from the others. Thus, research within the National Cancer Institute helped develop drugs now under trial in certain types of arthritis and related connective-tissue diseases. Further, work in progress on the "slow viruses" at the National Institute of Allergy and Infectious Diseases (NIAID) gives promise of explaining some forms of rheumatoid arthritis--the most prevalent and disabling variety which affects more than 4 million people in the U.S. NIAID, along with NIAMDD, also is attacking disorders of immunity that might likely be involved in rheumatoid arthritis.

Today, thanks to continuing research, much of which is Federally supported, the arthritis diseases are no longer looked upon as a life sentence of pain. Once considered virtually hopeless, these maladies now can be better managed and controlled, and suffering lessened. A notable case in point is gout, a very painful form of arthritis at one time partially controllable, and now highly manageable with drugs that regulate the chemistry of uric acid, the culprit in this disorder. Laboratory duplication--by scientists receiving Federal aid--of lysosomes (natural enzyme packages inside most body cells, including those that line the joints) holds exciting promise for further control of these crippling diseases.

NIH Clinical Center surgeons are using selected patients to study the value of synevectomy--the surgical removal of granulation tissue from the joint areas--in lessening the progressive destruction of cartilage and bone in rheumatoid arthritis. NIAMDD investigators continuously test scores of

(more)

drugs--from salicylates to potent corticosteroids--verifying the usefulness of gold treatments and new immunosuppressive agents. At East and West Coast centers, Government funds are supporting studies of one of the most dramatic surgical innovations in recent years--total hip replacement made possible by the discovery of cements so durable they make bone screws unnecessary.

The Administration is deeply committed to improving the health of the American people through the search for new knowledge on which all medical advancement is based. Under this commitment, arthritis research is and will continue to be a high-priority concern, with the best possible use being made of available resources. The Administration has recently endorsed collaborative US-USSR exploration into the nature and control of arthritis. At NIAMDD and various Government-supported research centers across the country, laboratory and clinical studies are proceeding vigorously on hundreds of projects directly related to arthritis. These endeavors continue to yield new diagnostic procedures, more effective therapies, improved long-term management techniques--all resulting in greater degrees of comfort and self-sufficiency for arthritis sufferers.

#

Medical News Tip

SCIENTISTS EVALUATE NUTRITIOUS FOODSTUFF--Acceptable, inexpensive protein-containing food products of high biologic value are badly needed to improve the nutrition of people in developing countries.

George G. Graham, Ph.D., of Johns Hopkins University has evaluated a recently developed "elbow" macaroni (GF-1) comprised of corn and soy and wheat flours as a source of inexpensive dietary protein for convalescent or acutely malnourished infants.

GF-1 has been described as having a moderately high-protein content, good digestibility, and high biologic value. The pasta-like substance has a protein content and quality higher than that of wheat flour and a cost lower than that of equivalent wheat products. Its acceptability has been proven by many populations, as demonstrated in Peru, Brazil, and the southern United States.

GF-1 could become an important weaning food, a main ingredient in school lunch programs, an excellent food for the elderly, or a highly nutritious component of any diet.

For further information about nutritious foodstuffs, contact:

Information Office
National Institute of Arthritis, Metabolism, and Digestive Diseases
Bldg. 31, Room 9A-04
NIH
Bethesda, Maryland 20014
Phone (301) 496-3583

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New Publication:
Venereal Disease

"VD is not a single disease...it's a whole collection of diseases."

With this statement, the new pamphlet, *Venereal Disease*, lists the various diseases--gonorrhea, syphilis, granuloma inguinale, nongonococcal venereal urethritis, chancroid, lymphogranuloma venereum, and certain viral infections such as Herpes Type 2.

The incidence of VD, once believed to be sufficiently controlled, has grown to epidemic proportions, especially gonorrhea and syphilis. According to this publication, increases can be attributed to complacency on the part of the public, a breakdown in cases reported to public health officials, the use of oral contraceptives, as well as other factors.

Venereal disease can be cured with penicillin if diagnosed and treated early enough. However, with the gonorrhea-causing organism developing a resistance to the drug, new methods for controlling the disease must be found. The pamphlet deals with research efforts initiated by the National Institute of Allergy and Infectious Diseases (NIAID) into the possible cures of VD. Synopses of the 17 projects are furnished.

The history of VD, as well as the future of NIAID-related research, such as gathering more information on the body's immunity to VD, are also detailed.

For additional information, contact:

NIAID Information Office
Bldg. 31, Room 7A-32
NIH
Bethesda, MD 20014
Phone (301) 496-5717

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News Releases Issued

(Summaries of NIH releases sent out since the last issue. For a copy of any of these, please write or call.)

BLINDNESS--Nonwhite women may be as much as three times more vulnerable to blindness from diabetic retinopathy than either white women or men of any race. This finding comes from an analysis of statistics on registered blind persons in 16 States compiled by the National Eye Institute. The study also shows that blindness rates in general are higher in these States among nonwhites than whites and that the greatest difference occurs in glaucoma. It is not certain, however, whether these apparent high rates of blindness among nonwhites are due to more complete registration among this population group or whether there actually is an increased risk of blindness for nonwhites. These findings are reported in the new publication *Statistics on Blindness in the Model Reporting Area, 1969-1970*.

CANCER CENTER--The National Cancer Institute (NCI) has renewed a research contract with Litton Bionetics, Inc. to manage, operate, and maintain the NCI Frederick Cancer Research Center at Fort Detrick, Frederick. This second-year contract will total $10,271,110. The Frederick Center was established in 1971, converting the former biological warfare facilities into a center for research on the causes, diagnosis, treatment, and prevention of cancer. Renovation and modification of the facilities were largely completed during the first year of operation. The renewed contract provides for ongoing research projects on viruses, chemical causes of cancer, biohazards containment, and drug development studies.

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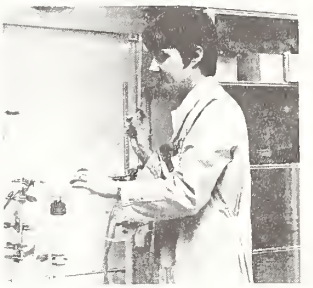
July 25, 1973



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NEWS & FEATURES From NIH July 25, 1973

Research Advances

DENTISTS DISCUSS ORTHODONTICS, CRANIOFACIAL ABNORMALITIES

The orthodontics of the future may try to alter an undesirable facial environment rather than rely primarily on tooth movement.

This new direction for research and therapy in malocclusion was recently reported by Charles J. Burstone, D.D.S., head of the Department of Orthodontics at the University of Connecticut School of Dental Medicine at Farmington.

Dr. Burstone, a grantee of the National Institute of Dental Research (NIDR), spoke at the Scientific Conference commemorating the 25th anniversary of NIDR, June 29, 1973, at the Washington Hilton.

According to Dr. Burstone, dentists--largely by trial and error--try to exert enough force to move teeth into better relations with existing facial proportions without harming the underlying tissues. Often, when these pressures are removed, the teeth slip back.

Dr. Burstone believes that it would be much better to learn how to stimulate bone growth piezoelectrically (that is, by small, pressure-induced changes in molecular charges) or to discover how to exert stronger orthopedic forces to remodel the parts of the face into harmony. If the face were proportioned properly, a minimum of orthodontic stress would be needed to shift teeth sufficiently to produce both attractive appearance and functional dentition.

The scientist explained that although approximately nine-tenths of all children have somewhat faulty tooth arrangements, only about 40% are sufficiently handicapped to require orthodontic treatment.

(more)

Orthodontics (Cont'd)

Dr. Burstone considers most malocclusion problems to be due to hereditary disproportions of bones or to the effects of bone responses to the pull of muscles in unfavorable or unequal functional patterns. For example, this can happen when the tongue pushes outward much harder than the lips pull inward.

According to the scientist, although malocclusion causes both physiological and psychological problems, it is not a disease in the usual sense because the tissues are healthy. Therefore, it has no preventable cause. Much more needs to be learned about facial growth, muscle stresses, and tissue responses to stress, Dr. Burstone warns, before treatment of malocclusion can become predictably successful.

The recent "marriage" of the computer with X-ray photography should improve such orthodontic treatment as well as cleft palate surgery to the benefit of the patient. According to Wilton M. Krogman, Ph.D., this new procedure has resulted in the ability to predict with considerable accuracy the facial features that a given child can be reasonably expected to develop as an adult in a given family, and the stages he must pass through.

Dr. Krogman, director of research for the Lancaster, Pennsylvania, Cleft Palate Clinic, spoke at the same scientific conference.

"We are already in the midst of a tremendous advance in craniofacial knowledge," Dr. Krogman explains. (He has spent over 40 years in study and research directed toward restoring a child born with a malformed face to a normal life style.) According to the scientist, this knowledge is being put to work along two fronts: *genetic*, in the analysis of abnormal growth in

(more)

syndromes; and *postnatal developmental*, in the clinical restoration of an orofacial disfigurement.

Dr. Krogman said the "quite literally we can, via precise (roentgenographic cephalometric) analysis, advise the surgeon and the orthodontist how to re-grow a face so that a distorted orofacial complex, under the surgeon's scalpel and saw, becomes 'normal' almost beyond belief."

He reports that he has seen ugly caricatures of a face re-designed, re-constructed, and re-functioned almost to the threshold of complete symmetry, harmony, and aesthetic acceptability.

Dr. Krogman also notes that the psycho-social problems of dento-facial disfigurement of various kinds are a health hazard affecting 20 percent of the adolescent population. Science has done good work with the body in craniofacial problems, he believes, but the psyche--the total personality of a total individual in a total cultural milieu--must also be taken into consideration.

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NOTE TO SCIENCE WRITERS: NIDR-supported work in the area of cleft palate research will be featured in a future "NIH Portfolio on Craniofacial Abnormalities."

Research Advances

DOCTORS FIND LONG HOSPITAL STAY UNNECESSARY FOR HEART PATIENTS

Patients with uncomplicated myocardial infarction derive no additional benefits from a three-week as opposed to a two-week hospital stay, according to results from a recent study. This finding could shorten the length of hospital stay for such cases.

The prospective, randomized, controlled study was conducted over a four-year period by physicians at Massachusetts General Hospital in Boston. It was partially supported by a contract from the National Heart and Lung Institute.

In earlier years, patients with uncomplicated but definite myocardial infarction were routinely hospitalized from four to six weeks. While a previous study showed that the necrotic myocardial region required a lengthy time to be transformed into firm scar tissue, still another study indicated that patients could be safely moved into a chair early after an infarction. Therefore, the necessity of a hospital stay of three to four weeks for uncomplicated myocardial infarction is based on little scientific data.

The investigators selected 138 patients for inclusion in the present study. Other patients were rejected because of complications of myocardial infarction, death from infarction, other medical problems requiring longer hospitalization, the occurrence of a previous myocardial infarction in the prior six months, and "social" reasons. The complications leading to exclusion included noteworthy ventricular arrhythmias, heart block, hypotension, congestive heart failure, and coronary pain.

(more)

Hospital Stay (Cont'd)

The investigators randomly paired the remaining patients into two groups of 69. Age and sex were comparable between the groups, and the only differences between them were attributed to previous cardiac conditions of individual members. However, there were no significant differences between the groups in the location of the infarction.

A prescribed activity schedule, with such mobility exercises as "dangle," "sitting in chair," and "walking," was assigned to patients in both groups. Exercises began a week into the hospital stay for the two-week group and 10 days into the stay of the three-week group, continuing for both until the day of discharge.

There was a significant deviation in the length of hospital stay for seven of the two-week and for two of the three-week patients. Three of the two-week and two of the three-week patients had extension of the myocardial infarction after the sixth day. In only one patient in each group did ventricular irritability later develop, requiring longer therapy. Discharge of three of the two-week patients was delayed because of noncardiac medical problems that subsequently arose. On the other hand, one three-week patient was inadvertently discharged early, and another signed out early against advice.

Patients in the two-week group were instructed to remain on one floor at home for two weeks after discharge, and those in the three-week group for one week. After this period (28th day after the infarction) instructions for progressive activity were identical for both groups.

Using standard evaluation forms, a study nurse and physician evaluated the patient's course on the 13th hospital day; on the day of discharge; and

(more)

at six, 12, and 24 weeks after the infarction. Physical findings, emotional stress, and functional capacity were all considered.

As a result, the investigators found that in the two-week group, three deaths occurred at a mean of eight weeks after the infarction; five subsequent infarctions occurred at a mean of seven weeks; and two episodes of subsequent acute coronary insufficiency requiring hospitalization occurred at a mean of 15 weeks.

On the other hand, of the 69 patients in the three-week group, there were five deaths occurring at a mean of seven weeks after the infarction, three subsequent episodes of infarction occurring at a mean of eight weeks, and three episodes of subsequent acute coronary insufficiency requiring hospitalization occurring at a mean of 15 weeks.

The investigators found that forty of the two-week patients returned to work in a mean of 12.4 weeks after the myocardial infarction, while 34 of the three-week patients returned to work in a mean of 13.8 weeks. Twenty of the two-week as compared to 26 of the three-week patients survived the six-month follow-up period without further hospitalization but did not return to work.

After the six-month study period, patients were asked to independently evaluate their course and follow-up data on each group of patients were compared statistically.

Paired analysis by three reviewers of the entire six-month course did not show any significant difference between the groups in terms of medical status, emotional status (with special attention to depression and anxiety) or overall functional status (taking into account both medical and emotional

(more)

factors). During the six-month follow-up period, there was no significant difference between the two groups in the rate of return to work, development of angina pectoris or congestive heart failure, aneurysm formation, incidence of acute coronary events, or death.

However, the investigators caution that proving that no significant differences between groups will be found with larger numbers or in subsequent trials is much more difficult than demonstrating the presence of significant differences.

Although the present study suggests that prolongation of hospital stay beyond two weeks confers no advantage on selected patients, the researchers make two qualifications. First, they advise that it is much harder to demonstrate the absence of a difference than the presence of one, because subtle differences might escape detection. Second, the results of the study apply only to patients with uncomplicated myocardial infarction. The researchers stressed individualization in the hospital care of patients after myocardial infarction rather than adherence to preconceived treatment plans.

This study was reported in the May 31, 1973 issue of the *New England Journal of Medicine* by Adolph M. Hutter, Jr., M.D.; Victor W. Sidel, M.D.; Kenneth I. Shine, M.D., and Roman W. DeSanctis, M.D.

This article was prepared by Jeffrey Christy, NIH summer information aide.

#

Research Advances

COLORADO TICK FEVER POSES NEW HEALTH HAZARD

Victims of Colorado Tick Fever (CTF) may be hazardous blood donors in the western United States and Canada where the disease is common. This warning comes from scientists at the Rocky Mountain Laboratory in Hamilton, Montana, a part of the National Institute of Allergy and Infectious Diseases.

Robert N. Philip, M.D., Elizabeth A. Casper, and Jack C. Cory detected the causative virus of CTF in a patient's blood nearly four months after he had recovered. This confirmed and expanded previous studies by other scientists who isolated the CTF virus from patients long after they had recovered. Dr. Philip and associates reported these findings at a joint meeting of the Professional Associations of the U.S. Public Health Service in Phoenix, Arizona, May 1973.

Colorado Tick Fever is an acute, usually self-limited, infection accompanied by fever, chills, headache, malaise, nausea, and occasionally vomiting. Although there is no specific therapy for it, complications rarely occur except in very young children.

The disease is widespread in the western states (see accompanying map). It reaches its peak incidence in June and July at higher altitudes and in April and May at lower altitudes. Almost anyone who camps, hunts, or fishes in this area is a potential victim of the bite of the wood tick, *Dermacentor andersoni*, which is the principal transmitter of the CTF virus.

While studying the disease, a staff member of the Rocky Mountain Laboratory inadvertently stuck himself with a needle contaminated with the CTF virus.

(more)

Tick Fever (Cont'd)

He became ill about four days later. In order to obtain as much information as possible about the virus-host relationship, Dr. Philip and his associates arranged to collect blood samples from the patient, beginning 48 hours after infection and continuing for 124 days from initial exposure.

The scientists detected the virus in the red blood cells of the patient from two to 100 days after infection. In contrast, it was present in the plasma only 10 days--during the acute clinical stages of the illness.

Involvement of the red blood cell system and persistent shedding of virus add a new dimension to Colorado Tick Fever as a health problem. Although the scientists do not have definite evidence the CTF is transmitted by blood transfusions, this seems to be a possibility. Although recipients of blood transfusions in the Rocky Mountain area are at greatest risk, CTF also poses a threat, to a lesser extent, in other parts of the U.S., since vacationers in the West may contract the disease and carry it home with them. Cases of CTF already have been recognized in such distant states as Florida and New York.

(more)

Tick Fever (Cont'd)

DISTRIBUTION OF WESTERN TICK

Shaded area represents distribution of Colorado Tick Fever.

#

NEWS & FEATURES From NIH July 25, 1973

Photo Feature

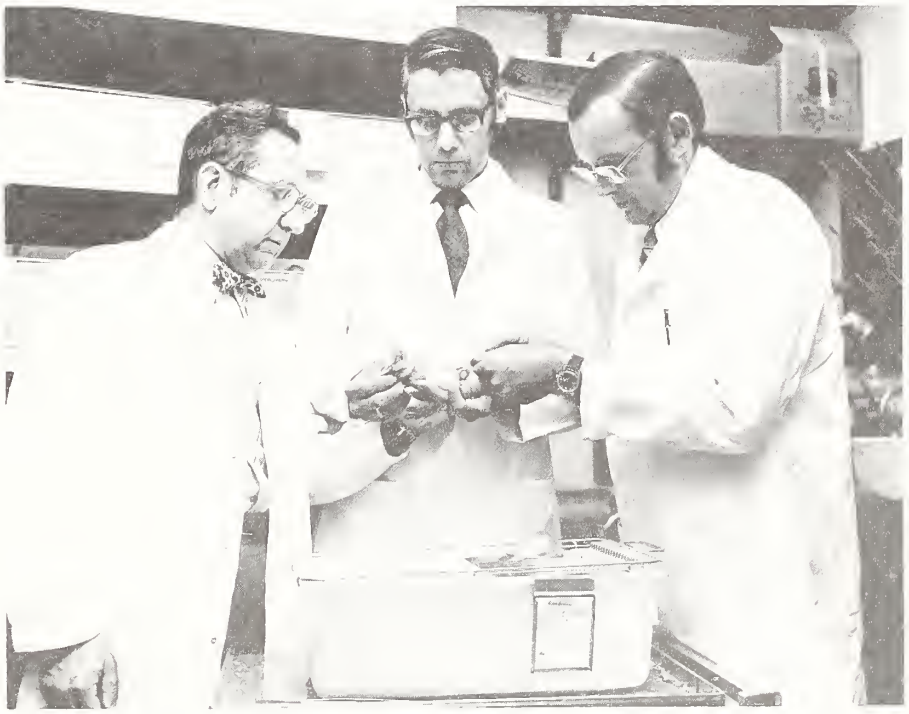
New Technique...

RAPID TEST CHECKS CHEMICALS FOR CANCER-CAUSING POTENTIAL

National Cancer Institute (NCI) scientists have developed a new method for rapid testing of chemicals for potential cancer-causing activity.

The technique, which tests chemicals by using animal embryo cells growing in a glass dish, may offer an efficient and economical procedure for the screening of thousands of environmental substances.

Environmental chemicals are currently tested for cancer-causing activity by feeding them to mice and rats throughout the animals' lives. Costly and time-consuming, each current test requires over 500 laboratory animals and



The NCI scientists inject a pregnant hamster with a chemical to begin a test of the chemical's effects. Shown (from left) are Joseph A. DiPaolo, Ph.D., Richard L. Nelson, and Charles H. Evans, M.D., Ph.D. (NIH Photo #1085)

(more)

two to four years to evaluate a chemical. NCI is presently testing over 400 chemicals, but it has determined the need to test tens of thousands of chemicals to which people are exposed.

The new method, which may indicate cancer-causing activity in as little as two weeks, is a modification of an earlier technique developed by NCI's Joseph A. DiPaolo, Ph.D., and scientists at other institutions.

The new procedure is described in the June issue of *Archives of Pathology* by Dr. DiPaolo, Richard L. Nelson, Paul J. Donovan, and Charles H. Evans, M.D., Ph.D., all of NCI's Biology Branch.

Under the new procedure, a test chemical is first injected into a pregnant hamster. The hamster embryos, exposed to both the chemical and its metabolic byproducts, are later removed and the embryonic cells grown in the test tube. Cancerous transformation is detectable when the cells are viewed under a microscope and confirmed by injecting the transformed cells into healthy hamsters where they produce cancers.

An earlier method consisted in applying a test chemical directly to cells from animal embryos growing in a glass dish to watch for signs of cancerous change. Because some chemicals cause cancer only after activation by metabolic processes in the body, their direct application to the cells may allow some hazardous chemicals to appear safe.

The scientists used the method to test 12 chemicals known to cause cancer, as well as five that do not. In each test four pregnant hamsters with average litters of 12-14 embryos were used. Each test correctly identified the cancer-causing potential of the chemical being evaluated.

(more)

New Technique (Cont'd)

Cancerous transformation in the embryo cells could be observed under a microscope within two weeks of their exposure to the hazardous chemicals. Usually three to 16 weeks are required for cancers to develop in healthy animals after injection with the transformed cells.

Further work is now planned by NCI using many other cancer-causing and non-cancer-causing chemicals to determine if such a method, requiring relatively few animals and few weeks, consistently detects cancer-causing activity. If its reliability is confirmed, Dr. DiPaolo said, the technique should aid greatly in the identification of environmental factors triggering cancer.

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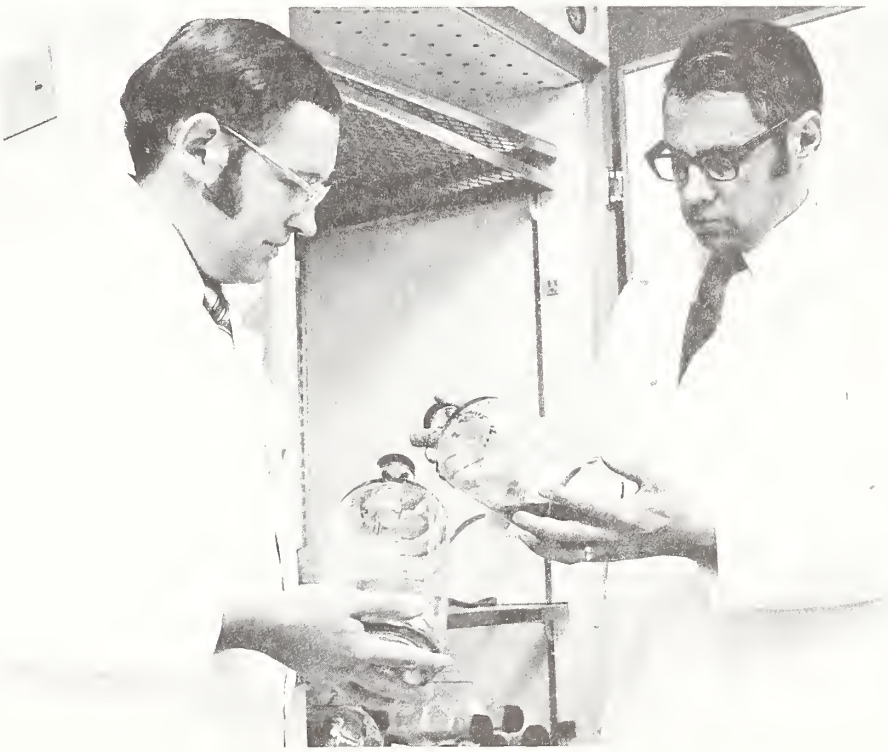
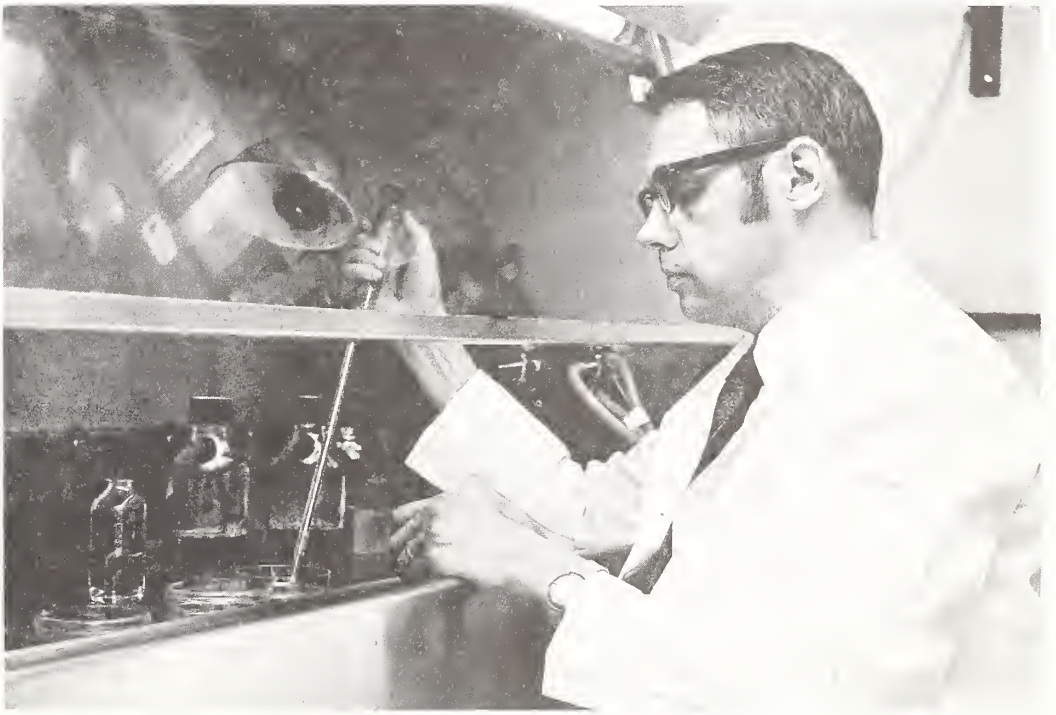


Fetal cells are removed from the test animals and stored in roller bottles in an incubator until the cells coat the bottles. Richard L. Nelson (right) and Charles H. Evans, M.D., Ph.D., are checking the progress of the cell coatings (NIH Photo #1086)

New Technique (Cont'd)

Joseph A. DiPaolo, Ph.D., is examining fetal cells as part of his microscopic studies in search of cancerous transformation. (NIH Photo #1087)



Working under a laminar flow hood, Richard L. Nelson treats embryonic cells with chemicals. (NIH Photo #1088)

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News Feature

RESEARCH BRINGS NEW HOPE FOR ONCE-DOOMED CHILDREN

Today there is fresh hope for eventual control of the leading fatal disease of American children. Thanks to research advances, children with acute leukemia treated with drug combinations are living more than 10 times longer than before. Some of them are even being cured. Life-saving techniques are being extended to more U.S. medical centers than was possible before.

Eight comprehensive cancer research and development centers authorized by the National Cancer Act of 1971 were established throughout the U.S. recently; seven others will be added by July 1, 1974. And seven or eight medical centers will begin "Cancer Control" projects to demonstrate new treatment methods, and to shorten the time before their wide adoption in medical practice.

Modern leukemia therapy had its start in 1947 when the late Sidney Farber, M.D., and others at the Children's Cancer Research Foundation, Boston, used a now outdated drug to produce the first temporary lessenings of disease in children with acute leukemia.

In the mid-1960's the National Cancer Institute (NCI) mobilized a corps of top scientists into Federally-funded cooperative groups to work out the new leukemia treatment techniques that are producing today's improved results. The task was not easy. Only a few drugs were available by then, but information on how to use them effectively was scant.

(more)

Leukemia (Cont'd)

Gains were made by inches. This special breed of scientists knew--and accepted--that each new drug would add only a few months to the life of a child. And they knew that the drugs themselves, like the disease, often stripped the child's bone marrow of blood elements needed for survival.

In acute lymphocytic leukemia (the type of leukemia most common among children) abnormal white cells flood the youngster's bloodstream. They crowd out essential red cells and the child becomes anemic, pale, and listless. The disease also reduces the number of blood platelets--the sticky little particles that help the blood to clot. As a result, a relatively minor cut or scratch may cause excessive bleeding that threatens the child's life. Special cells called granulocytes, that protect against infection, become dangerously scarce.

To replace these essential blood elements, concentrated transfusions of blood platelets and infection-fighting granulocytes were needed.

To develop instrumentation for such specialized transfusions, NCI entered into an agreement with the IBM Corporation. After several years the team succeeded. Today, at the major leukemia treatment centers, an IBM blood cell separator is a basic part of the supportive care system that helps leukemia patients overcome their disease, sometimes permanently.

To provide relatively germfree hospital environments for patients with leukemia and certain other diseases, once again the NCI turned to industry. An early system, called the "Life Island," enclosed the patient's bed in a protective plastic bubble. Further research led to creation of the so-called "laminar-flow room." Here, a patient breathes air continuously filtered and

(more)

Leukemia (Cont'd)

virtually germfree. Visitors and hospital personnel remain "downwind" of the patient, and present no hazard in the laminar flow of air.

Even more promising approaches are evolving. For example, a prototype "spacesuit" is being designed so that hospitalized patients can have more freedom of movement about the hospital, yet remain protected from harmful bacteria or viruses.

Despite their technical brilliance, and the immediate gains from such devices, the final payoffs will probably come from more fundamental research. For example, studies of cell chemicals, such as the nucleic acids that make up genes, may provide clues to the design of new drugs.

At present, eight drugs are useful. Combinations of two, three, and four drugs usually result in complete--but often temporary--disappearance of disease for children with acute leukemia.

Some of the most promising results thus far have been reported by scientists at the St. Jude Children's Research Hospital in Memphis, Tennessee, supported in part by Federal funds. Doctors there have reported three-year continuous remissions (the disappearance of all evidence of disease) among 61 percent of a group of children with leukemia. In addition to receiving drug combinations, the children were treated with radiation early in the course of their remissions. Investigators at that center, reviewing their results, now suggest that acute lymphocytic leukemia should not be viewed as an inevitably fatal disease.

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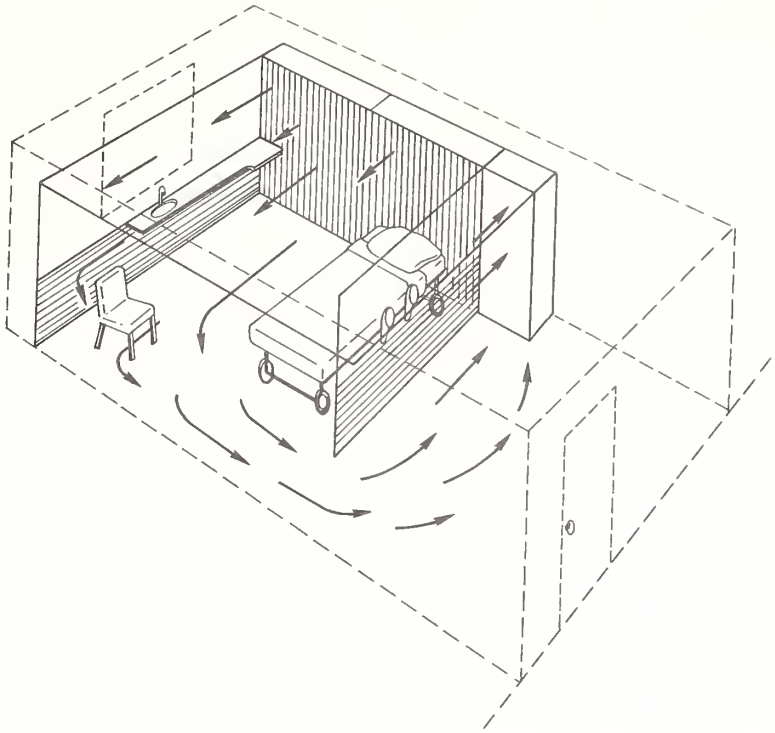
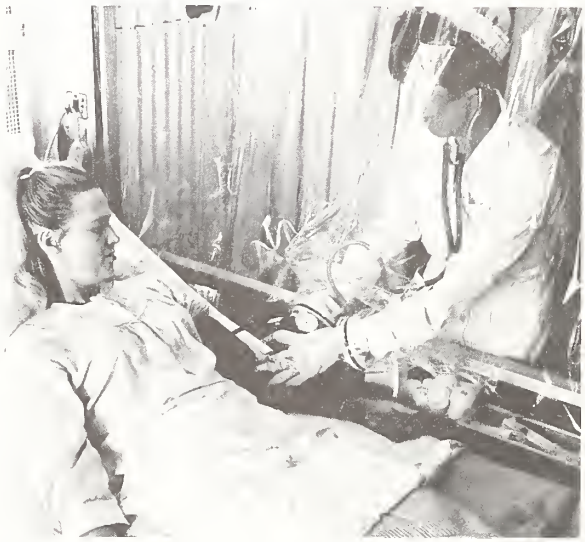
Leukemia (Cont'd)



A new portable laminar air flow unit (wall at head of bed) continuously recirculates ultra-clean air in an ordinary hospital room. NIH scientists in the National Cancer Institute, who developed this relatively germ-free system, are testing it on chemotherapy patients at the NIH Clinical Center. (NIH Photo #1089)



Nursing attention for patients confined to a virtually germ-free room is accomplished without risk of infection. A nurse can place her hands into gloves that are attached to the acrylic wall. The new portable laminar air flow unit was developed by NIH scientists at the National Cancer Institute. (NIH Photo #1090)

#

Women in Research... Photo Feature

UNIVERSITY OF TEXAS RESEARCHERS PROBE THE BIOMEDICAL SCIENCES

These four women scientists are among the NIH grantee researchers who are faculty members of the new Graduate School of Biomedical Sciences at the University of Texas Health Science Center, Dallas. Bettie Sue Masters, Ph.D. (above left), is shown doing a chromatographic purification of enzymes and antibodies. The National Heart and Lung Institute supports her work in drug metabolism. At the microscope (above right) is Eleanor R. Siperstein, Ph.D., whose investigation of the cells producing ACTH (adrenocorticotropic hormone) is funded by the National Institute of Arthritis, Metabolism, and Digestive Diseases. (NIH Photos #1091, 1092)

(more)

Texas Researchers (Cont'd)

Mary E. Gaulden, Ph.D. (above), is studying chromosome mutations induced by diagnostic radiation in children. The National Institute of Child Health and Human Development is supporting this work. Kathryn V. Holmes, Ph.D., uncrates her new electron microscope. Her work under a National Cancer Institute grant includes studying the interactions between viruses and cell membranes with special emphasis on the groups of viruses that can cause cells to fuse into giant, multinucleated cells. (NIH Photos #1093, 1094)

#

Medical News Tip

HIGH BLOOD PRESSURE--The High Blood Pressure Information Center (HBPIC) oversees public and professional information about hypertension.

The Center, a branch of the National Heart and Lung Institute's Office of Information, is part of the National High Blood Pressure Education Program (NHBPEP).

Begun last year, the NHBPEP has become the coordinating unit for research efforts aimed at preventing thousands of deaths annually from high blood pressure. Hypertension can be controlled with the proper medical care, but it can lead to death from heart failure, stroke, and renal disease if neglected. A key element in the developing national campaign against hypertension is education, both public and professional.

In addition to NIH, other Federal agencies involved in NHBPEP are the Food and Drug Administration, the Veterans Administration, and the Department of Defense. In the private sector, the American Medical Association, National Medical Association, and the American Heart Association are committed to checking the risks of hypertension.

The address of the HBPIC is:

National High Blood Pressure Information Center
120/80 National Institutes of Health
Bethesda, Maryland 20014

The numbers in the address represent what is considered a normal blood pressure reading.

#

Capsules

(With this issue we begin a series of short news items.)

HYPERTENSION--Hypertension, or high blood pressure, afflicts at least 23 million Americans, reports the National Institutes of Health. High blood pressure increases a person's risk of having a heart attack, stroke, or developing kidney disease.

HUMAN BODY--The mature human body is the end result of nearly 20 years of growth. Each individual begins as the product of two cells and eventually is made up of 100,000 billion cells, according to the National Institutes of Health. The most rapid and crucial period of growth in the human being occurs in the nine months before birth.

COMPUTERS--Computers at the National Institutes of Health can monitor a post-surgery patient's heart rate and blood pressure 200 times a second.

CATARACT SURGERY--Cataract surgery is one of the most successful operations performed today. From 90 to 95 percent of patients undergoing this operation regain useful vision, reports the National Institutes of Health.

LEUKEMIA--Leukemia is cancer of the blood-forming organs and is characterized by uncontrolled production of abnormal white blood cells. Leukemia may strike at any age, develops each year in about 19,000 Americans, and kills about 15,000, according to the National Institutes of Health.

(more)

Capsules (Cont'd)

LARGEST LIBRARY--The world's largest library in a single scientific field is the National Institutes of Health's National Library of Medicine. The Library houses nearly 1.5 million books, journals, and other materials.

TOOTH DECAY--Only two percent of Americans escape tooth decay for a lifetime, according to the National Institutes of Health. Also, American mouths probably contain one billion unfilled cavities at any time.

#

New Publication:
Malaria

"Malaria, one of the oldest and most devastating plagues of mankind, remains one of the most common infectious disease in the world."

An understatement to be sure when the pamphlet, *Malaria*, continues with the astonishing fact that more than one billion people live in areas where malaria is a direct health threat.

Malaria is caused by the organism, Plasmodium parasite. Of the fifty types of malaria caused by this organism, only four prey on man--vivax, falciparum, and less commonly, malariae, and ovale.

This new publication tells the symptoms of the disease--often and disastrously mistaken for influenza--and stresses the need for early diagnosis. A history of drug therapy and treatment, from the basic quinine solution to the newer synthetic antimalarial drugs, is also provided.

A malaria life cycle chart is illustrated, showing the development and transmission of the malaria parasite from the mosquito to man. Efforts to prevent malaria by eradicating mosquitos with insecticides such as DDT are discussed, although mosquito resistance to DDT has become prevalent.

Current and future research efforts into malaria and mosquito control, initiated by the World Health Organization, the Center for Disease Control in Atlanta, the Walter Reed Army Institute of Research in Washington, D.C., and the National Institute of Allergy and Infectious Diseases (NIAID), are detailed in the new publication.

Science writers may obtain a free copy of this publication from:

NIAID Information Office
Bldg. 31, Room 7A-32
NIH, Bethesda, MD 20014
Phone (301) 496-5717

#

News Releases Issued

(Summaries of NIH releases sent out since the last issue. For a copy of any of these, please write or call.)

DEMONSTRATION PROJECTS--The most effective treatments for three types of cancer will be made more widely available in the United States through approximately 120 hospitals in seven contract-supported demonstration projects. Acute lymphocytic leukemia, Hodgkin's disease, and non-Hodgkin's lymphomas have been chosen for the demonstration program because recent advances in treatment--particularly with anti-cancer drugs--have greatly improved survival times for patients receiving such treatment. Seven "primary" hospitals will act through regional networks of "contributing" hospitals to demonstrate the most helpful treatments for these diseases. The regional programs are intended to deliver the best possible cancer treatment at the community level to patients who would not otherwise have access to such treatment.

ANIMAL FACILITIES--Six new grants, for renovations and improvements of laboratory animal facilities, were recently issued by the Division of Research Resources. Designed specifically to aid research institutions to meet the requirements of the Animal Welfare Act of 1970 and the DHEW policies on care and treatment of laboratory animals, the facility improvement program administered by DRR's Animal Resources Branch now includes 28 projects. The improvements involved may include purchase of equipment such as cages, cagewashers, and autoclaves; minor repairs to facilities; and some support for key personnel needed to upgrade the management and technical competence of the laboratory animal facility.

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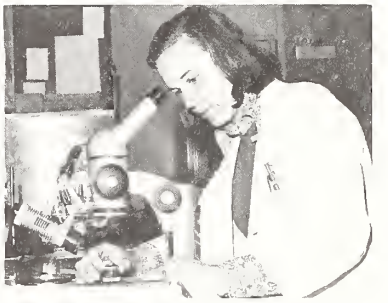

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Phone: (301) 496-1206

Research Advances

Increased Tooth Decay...

PROTEIN DEFICIENCY STUNTS RAT GROWTH

Protein deficiency during gestation and lactation not only stunts growth but also significantly increases susceptibility to tooth decay, according to studies done with rats by Juan M. Navia, Ph.D., and Lewis Menaker, D.M.D., Sc.D., of the University of Alabama Institute of Dental Research in Birmingham. The Alabama Institute is supported by funds from the National Institute of Dental Research (NIDR).

These studies suggest that protein deficiency coupled with increased sugar consumption could account for the rising incidence of tooth decay occurring throughout the world. As people migrate to cities and as civilization brings sugar to previously-isolated regions, many people on low protein diets face premature loss of all their teeth through caries breakdown.

Previously, the scientists had shown that protein-deficient rats produce offspring which are highly susceptible to tooth decay. But because the inadequate diet decreases only the amount of the nursing mother's milk, and not its quality, the results could have been attributed to an overall under-nutrition. In the current studies, some of the rat pups were hand fed a protein supplement and others a supplement with equivalent calories, vitamins, and minerals but without protein. The investigators gave the supplements during the lactation period so that the effects of protein on tooth development could be measured. The animals, which are no larger than a man's thumbnail,

(more)

Protein Deficiency (Cont'd)

were fed by means of a syringe with a bulb-tipped needle twice a day. After weaning, all animals were given a protein adequate, but caries-promoting diet containing sugar.

The experimental design enabled the scientists to separate the effect of protein from those of caloric malnutrition during tooth development. Protein supplementation during tooth development reduced caries to the low level seen in the consistently well-nourished animals. On the other hand, the protein free supplement did not protect the rats from rampant decay.

(more)

Rat pup, held between the investigator's thumb and forefinger, is being fed with a bulb-tipped needle to supplement the milk it receives from nursing. Studies with these tiny rats are conducted by Drs. Juan M. Navia and Lewis Menaker at the University of Alabama. (NIH Photo #1096)

Shown here are two "healthy" rats of the same age bred for NIDR-supported studies of protein deficiency. Stunted growth in the smaller rat is attributed solely to protein deficiency during lactation. (NIH Photo #1095)

Protein Deficiency (Cont'd)

At weaning, offspring of protein-deprived dams weighed only about half as much as offspring of dams given a 25 percent protein diet. With protein supplementation during lactation and a nutritious diet thereafter, animals were able to achieve 90 percent of the control weights, while animals not given the supplement during the nursing period could achieve no more than three quarters of the control weights.

The investigators ruled out the possibility that protein deficiency delays tooth eruption enough to increase decay because it exposes the highly-susceptible, newly-erupted tooth to high sugar diet instead of to mother's milk. They found eruption was delayed too briefly (only one day) to account for the difference in decay rates. Even when exposure to the diet was equalized by weaning protein-supplemented pups one day earlier than the protein-deprived animals, the well-nourished ones had significantly less tooth decay than did the deficient ones.

The scientists hope to learn whether protein deficiency makes the tooth structurally weaker or makes the salivary protective system less efficient. The team has found that protein deprivation decreases the DNA, RNA, and protein production in cells of major salivary glands as well as the number of cells. They also found that low cell count can be reversed by dietary supplementation during development.

These studies were described at the 1973 meeting of the International Association for Dental Research held in Washington, D.C., in April 1973.

#

Research Advances

First Report...

LIGHTNING DAMAGES EAR, MAY RESULT IN DEAFNESS

Although lightning kills approximately 300 persons in the United States each year, a much larger number survive the incident. Most people recover without after affects, but the violence of the lightning may cause severe damage to the ear.

LaVonne B. Bergstrom, M.D., and associates at the Division of Otolaryngology of the University of Colorado Medical Center, Denver, have been studying the lightning-damaged ear and the edema, sensorineural hearing loss, hemorrhage, and other conditions caused by it. Dr. Bergstrom's recent paper on the subject marks the first time that anyone has put together information about lightning damage to the ear. Previously, information gained from experiences of otolaryngologists has been transmitted by word-of-mouth only. No articles in otolaryngology journals can be found on the subject.

Dr. Bergstrom, whose work was funded by the National Institute of Neurological Diseases and Stroke, began his study by examining reports of lightning victims as far back as 1888. One such case study recounts the history of two wood-cutters struck by a bolt of lightning as they sat under a tree eating lunch. One man, stunned and burned, recalled crawling to the road calling for help and being somewhat deaf.

His friend, upon regaining consciousness, "could not hear a watch tick when laid to his ear or held between his teeth." Three weeks later he developed ringing in the ears and experienced a sudden discharge of pus from both ears.

(more)

Lightning (Cont'd)

Dr. Bergstrom reports that in 1941 an elderly woman, whose main injury from lightning was to her ear and mastoid bone, had the right external ear almost torn away and the upper one third struck off by lightning. Bloody spinal fluid dripped from the ear canal for seven days and almost complete nerve deafness was found even though the right ear drum healed. Other cases show similar findings.

In his article, Dr. Bergstrom also reports on four of his own case studies. One is the account of a 46-year-old male who was thrown off his tractor by a bolt of lightning. Three other case studies describe the clinical manifestations of men who were struck by lightning on the golf course. An autopsy was performed on the body of the man who died after five days in order to determine the amount and type of damage to the ear.

All the cases where the men survived showed temporary unconsciousness accompanied by retrograde amnesia and followed by ear hemorrhage, perforated ear drums, sensorineural hearing loss, and edema of the auditory canal. A ringing in the ears was usual. The hearing loss was usually partial and temporary, but permanent total losses have been reported in the past.

To understand how lightning damaged the ear, Dr. Bergstrom and associates investigated electrical impact on the ear. In the literature, they found studies of animals showing that high voltage electrical impact causes a rupture of the tympanic membrane with bleeding into the middle ear, cochlea, and cochlear aqueduct.

The approximate electrical potential of a lightning bolt is 20,000,000 volts. The extent of injury to a person struck depends on the power, the position and grounding of the person, and the duration site of entry and exit.

(more)

Lightning (Cont'd)

Injury to vital function caused by electrical shock varies a great deal with the path of current. The electric current passes through the body as though it were a gel, choosing the shortest path from contact to contact.

The temporal bone pathology of Dr. Bergstrom's cases suggests two possible mechanisms of injury, perhaps occurring simultaneously--blast effect and direct effect. It is possible that lightning entered the ear by two routes, both the external auditory canal and the internal auditory canal, because the structures between these two canals were undamaged.

As a suggestion for treatment, Dr. Bergstrom proposes delaying treatment of the lightning victim until it is known whether the ear drum will heal on its own and whether there is vascular damage. Until normal-appearing vascular tissue is restored by healing, premature reconstructive surgery of the middle ear may fail.

Dr. Bergstrom recommends surgical repair of the tympanic membrane in patients whose ear drums have not healed within six months to a year. According to the investigator, a patient should be observed periodically to show if there is necrosis or discontinuity of the bones of the ear.

Dr. Bergstrom and associates Lewis M. Neblett, M.D., Isamu Sando, M.D., William G. Hemenway, M.D., and Gerald D. Harrison, M.D. presented these findings at the Medical Audiology Workshop, held in Vail, Colorado, March 6, 1973.

#

This article was prepared by Anne Sexton, NIH Summer Information Aide.

Research Advances

In the Literature:
Pediatric Research, March 1973

CORNELL DOCTORS FIND NEW HOPE FOR VICTIMS OF BILIARY ATRESIA--Biliary atresia, a rare illness which affects one out of every 25,000 newborns, may become rarer still due to a new approach developed by a research team in New York City. The team includes Norman B. Javitt, M.D., associate professor of medicine and head of the Gastroenterology Division and collegues at the Cornell University Medical College. Dr. Javitt is a grantee of the National Institute of Arthritis, Metabolism, and Digestive Diseases.

Biliary atresia is the term used to describe the condition of infants who are born without functioning bile ducts. These children usually die after several years because of resultant cirrhosis. Cholestatic syndromes such as biliary atresia--that is, those diseases characterized by the stoppage of bile--represent a difficult diagnostic and therapeutic problem for patients of any age.

In his studies, Dr. Javitt found that many children who seem to have biliary atresia have instead another condition--a metabolic flaw that reduces the capacity to make bile. Because of this, Dr. Javitt explains, the bile ducts are underdeveloped--in fact they can be so small that they may not be recognized at surgery. Often, these children can be treated by medications that correct the metabolic insufficiency and so permit the ducts to develop.

Dr. Javitt and colleagues began their study with seven infants and children at the New York Hospital who suffered from biliary atresia. Five of the children have been followed since birth and two entered the program at two years of age.

(more)

Biliary Atresia (Cont'd)

Later, Dr. Javitt enlisted the cooperation of Lawrence Gartner, M.D., at the Albert Einstein College of Medicine, and Melvin Hollander, M.D., of Fordham Hospital to increase to 25 the number of patients who could be studied.

In their investigation, the Cornell doctors developed a new method of analyzing minute amounts of bile salts in blood. This replaced an older method which required taking undesirably large amounts of blood from the newborn. The new method, which is effective with as little as 0.25 milliliters of blood, permits precise determination of each of the bile salts by gas-liquid chromatography.

At present, five patients are being treated at the New York Hospital-Cornell Medical Center--one since birth. According to Dr. Javitt, all are doing well on therapy.

Dr. Javitt and colleagues Kevin P. Morrissey, M.D., Elliot Siegel, M.D., Henry Goldberg, M.D., and Ms. Engeline Kok, published a full report of their findings in *Pediatric Research*, March 1973.

#

NEWS & FEATURES From NIH August 10, 1973

Photo Feature

SCIENTISTS INVESTIGATE REPRODUCTIVE BIOLOGY

The University of Pennsylvania School of Medicine is conducting a special study of reproductive biology in a program project supported by the Center for Population Research of the National Institute of Child Health and Human Development (NICHD).

The study emphasizes the intraluminal environmental conditions within the female reproductive tract prior to implantation of the embryo. It includes investigation of the physiologic, biochemical, and biosynthetic mechanism involved in regulation of the menstrual cycle; physiology and transport of sperm; fertilization and mechanism of implantation; physiology of conception; and the assay and role of hormones in early pregnancy.

Luigi Mastroianni, Jr., M.D., professor and chairman of the Department of Obstetrics and Gynecology, is the principal investigator of the program project at the University of Pennsylvania.

The NICHD Center for Population Research is searching for new techniques for fertility regulation and for the alleviation of infertility, according to Philip A. Corfman, M.D., Center Director.

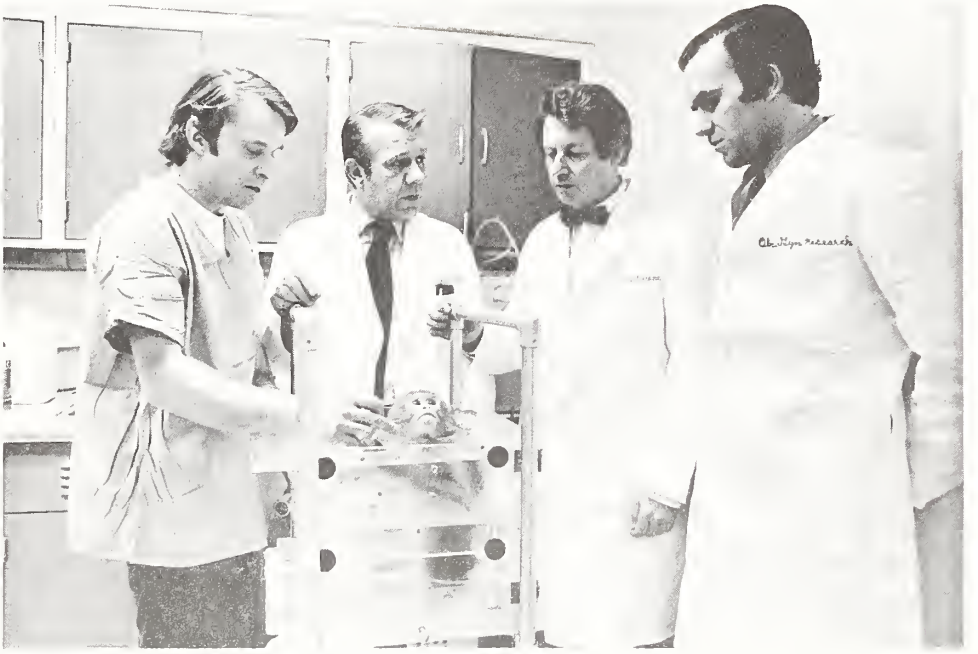
(more)

Reproductive Biology (Cont'd)

Luigi Mastroianni, Jr., M.D. (left photo) withdraws oviduct fluid from the collection chamber of a rhesus monkey during NIH-funded studies of reproductive biology at the University of Pennsylvania School of Medicine. In the photo at right, Francisco Floriani, M.D. (left) and H. Michael Seitz, Jr., M.D. remove the oviduct fluid collection chamber. The reproductive biology research is supported by the Center for Population Research, NICHD. (NIH Photos #1097, 1098)

(more)

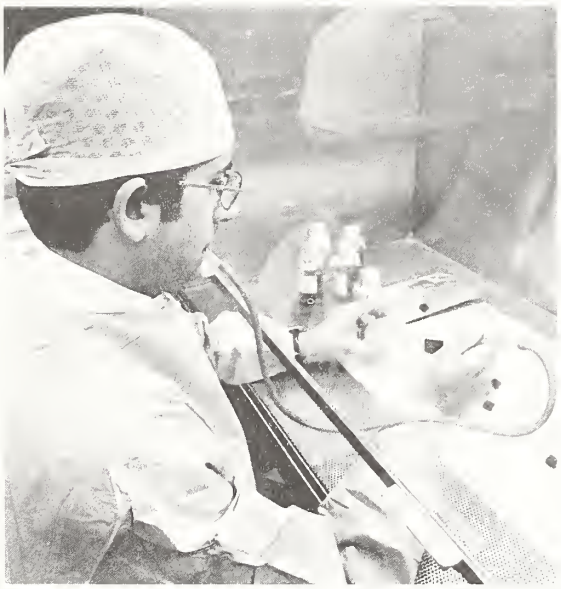
Reproductive Biology (Cont'd)



Animal studies are part of the research into reproductive biology conducted at the University of Pennsylvania School of Medicine. In the above photo, (from left) Charles I. Meltzer; H. Michael Seitz, Jr., M.D.; Luigi Mastroianni, Jr., M.D.; and Francisco Floriani, M.D. check the progress of a chamber monkey. In the photo at right, Luis Blasco, M.D. (left) and Howard Carter study the reproductive organs in an anesthetized rabbit. (NIH Photos #1099, 1100)

(more)

Reproductive Biology (Cont'd)



Various techniques are involved in the study of reproductive biology at the University of Pennsylvania School of Medicine. Bayard Storey, Ph.D., (top photo) uses a miniature oxygen electrode for polarographic assay of respiratory activity of sperm. Santo V. Nicosia, M.D. (left photo) prepares media for tissue culture of granulosa cells and follicular oocytes. Shown at right is part of the process of flushing the ovary of a rhesus monkey. The National Institute of Child Health and Human Development supports the reproductive biology research. (NIH Photos #1101, 1102, 1103)

#

Photo Feature

Glaucoma Research...

NEI STUDIES LEADING CAUSE OF BLINDNESS

Visual disorders rank high among the causes of disability in this country. By a conservative estimate, there are at least a third of a million people in the United States who are legally blind. Almost ten million people are visually impaired and, of these, over 1.3 million are unable to read ordinary newsprint with either eye, even with glasses.

Thanks to special education, vocational rehabilitation, and technological aids--and most of all through personal dedication and perseverance--many visually handicapped people are able to lead happy and productive lives. But for others, such as the elderly and multiply-handicapped, vision problems can be devastating, both psychologically and physically.

Federal and State governments and private agencies spend almost half a billion dollars each year to aid those legally blind people who require such assistance. The yearly cost of blindness to the nation, in terms of lost or limited productivity, is approximately $800 million.

The economic dimensions of blindness are, of course, a poor measure of the human and social aspects of this problem. But such statistics do help quantify this problem and underscore the importance of undertaking preventive efforts, both for improving health and reducing dependency.

In mounting its research attack on visual disability, the National Eye Institute (NEI) has sought to determine where the greatest opportunities lie for significant progress within the next few years. Glaucoma was selected, from among the most common visual disorders, as the area where applied

(more)

research and development projects are most likely to achieve practical results.

Glaucoma is a leading cause of blindness and visual disability and experts advise us that a strong base of scientific information already exists on which a program of applied research can be built. Furthermore, sufficient trained manpower is available to undertake such an effort.

Glaucoma occurs when the fluid pressure within the eye is high enough to damage the optic nerve. The disease usually develops painlessly and gradually so that visual loss may go unnoticed by the victim until it is far advanced. Although glaucoma cannot be cured, it can usually be controlled by regular and frequent medication, mostly in the form of eye drops, which keep the pressure under control. Most glaucoma patients can expect to retain useful vision for the rest of their lives if they remain under medical care and use their medication regularly.

If such is the case, then why does this condition take such a great toll in blindness and disability? The answer to this seeming paradox lies both in the nature of the disease and in the current methods of treatment.

The early stage of glaucoma is almost always detected by routine eye examinations or mass screening programs. A number of victims seek medical attention only after they have lost a significant amount of vision.

Another problem lies with the drugs now available for treatment. While there can be no doubt that the preparations currently in use have saved many from blindness, many patients find them unpleasant, worrisome, and expensive. The need for a patient to use eye drops several times daily is another drawback.

(more)

Glaucoma Research (Cont'd)

Surgery is used for glaucoma when drugs do not control a patient's eye pressure and loss of sight is imminent. However, glaucoma surgery is not successful in all cases and there is great need for more effective methods.

At present, glaucoma screening consists of measuring the fluid pressure within the eye. This technique is useful but inefficient, since elevated pressure does not always appear to lead to visual loss. NEI is now supporting investigations of techniques to give more direct and efficient screening for glaucoma, rather than just for high pressure.

Evaluation of new drugs and studies of the action of present ones are also under way, both by the National Institutes of Health scientists and those in non-government research institutions working with Federal support. New ways of administering medication are being developed. By using a drug-impregnated plastic device which fits under the lower eyelid, it may be possible to deliver medication continuously to the eye without the need for frequent administration by the patient

New surgical techniques are also being sought. Experiments with lasers are under way and other techniques, such as the use of powerful enzymes to unblock the flow of fluid through the eye, are being studied.

(more)

Schiotz tonometer is used to measure pressure within the eye in glaucoma screening. Procedure is painless and takes only seconds. (NIH Photo #1104)

Glaucoma Research (Cont'd)

Even the possibility of reversing early visual loss in glaucoma is being explored, NEI-supported basic research has given scientists a theoretical basis for restoring damaged optic nerve cells. Studies are now under way to determine the practicality of accomplishing this in patients.

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Photo Feature

Women In Research...

NIAMDD PROVIDES SUPPORT FOR SCIENTISTS
AT MANY UNIVERSITY MEDICAL SCHOOLS

At the Washington University School of Medicine, Sondra Schlesinger, Ph.D., (left) associate professor of Microbiology, sets up a gradient electrophoresis column. Her work, supported by the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD), may lead to a better understanding of the control of synthesis of proteins in the cell. (NIH Photo #1105)

Constance Shen Pittman, M.D., an NIAMDD grantee and professor of Medicine at the Georgetown University School of Medicine, is researching the actions and metabolism of thyroid hormones. (NIH Photo #1106)

(more)

NIAMDD Grantees (Cont'd)

Dorothy Ford Bainton, M.D., assistant professor of Pathology in Residence at the University of California, San Francisco (UCSF), is shown at the dissecting microscope. Her NIAMDD-supported work is designed to provide new information on the defects which occur in differentiation of leukemia cells and elucidate the mechanism responsible for their inability to function as normal cells in defending the body against bacterial invasion. (NIH Photo #1107)

Carolyn F. Piel, M.D. (above), is an associate professor in Pediatrics at UCSF. Her NIAMDD-supported research involves the study of renal disease in childhood. From left to right in the photo: Dr. Piel; Dr. Diane Ware, a fellow in pediatric immunology; and Marian Weeks.

Leah M. Lowenstein, M.D., Ph.D. (right), at the Boston University School of Medicine, examines a tracing from an automatic amino acid analyzer. Her NIAMDD-supported work is designed to determine the causes of renal failure in liver disease and investigate the mechanism of renal compensatory growth. (NIH Photos # 1108, 1109)

#

Medical News Tip

KNEE JOINT REPLACEMENT--The development of two different types of knee prostheses and of a rapid setting bonding cement, methyl metharcylate, is providing physicians with better techniques for treatment of rheumatoid and other forms of arthritis.

Supported by the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD), Gerald A.M. Finerman, M.D., head of the team at the University of California at Los Angeles, in addition to research teams from four other medical centers, have replaced 300 knee joints severely damaged by osteoarthritic or rheumatoid arthritis with encouraging results.

Two hundred patients have received the concentric total knee prosthesis, and 100 have received a geometric prosthesis. The latter conforms not to anatomic outlines, but to geometric lines of force.

Total knee replacement in aged patients has provided, in almost every instance, relief of pain and sufficient function to permit basic daily activities previously denied.

It is anticipated that the Food and Drug Administration will soon approve methyl metharcylate for general use in knee surgery. About three years ago, this acrylic bonding was approved for total hip replacement.

For additional information, contact:

NIAMDD Information Office
Building 31, Room 9A-04
NIH, Bethesda, MD 20014
Phone (301) 496-3583

#

Capsules

RETINAL DETACHMENT--Retinal detachment is a separation of the inner from the outer layer of the retina, the light-sensitive tissue at the back of the eye. The National Institutes of Health reports that this condition, which can cause permanently impaired vision, occurs most commonly in men, the very nearsighted, and the aged.

METABOLISM--Metabolism is the amazing process whereby the body biochemically transforms food into tissue elements and into energy for growth, repair, and general body functions, according to the National Institutes of Health.

PSORIASIS--Nearly eight million Americans have the reddish patches of skin called psoriasis. Psoriasis is hereditary and only one parent need be affected for a child to develop psoriasis, according to the National Institutes of Health.

ARTIFICIAL KIDNEY--A new type of artificial kidney requires only about a half-gallon of recirculating fluid to help cleanse the blood of impurities reports the National Institutes of Health. Also, the new machine eliminates costly plumbing and water-purification systems. Formerly, a single dialysis treatment required 80 to 100 gallons.

NORMAL VOLUNTEERS--By studying healthy volunteers at the National Institutes of Health Clinical Center, scientists gain insights into body functions in disease. The normal volunteers are often from church groups, civic organizations, and student groups.

CAPSULES (Cont'd)

ELECTRON MICROSCOPES--The invention and refinement of the electron microscope has been the most dramatic development in modern microscopy, according to the National Institutes of Health. The electron microscope has enabled scientists to delve further into the structure of cells.

SICKLE CELL--In the United States, sickle cell trait occurs in about two million black people. Sickle cell anemia, the severe form of the sickle cell problem, affects about 50,000 blacks, who may undergo painful episodes called sickle cell crises, reports the National Institutes of Health.

DENTAL PLAQUE--Dental plaque is a colorless, transparent film on the teeth made up of saliva and bacteria materials. The National Institutes of Health reports that plaque contributes to tooth decay, and is also an agent in the cause and development of periodontal disease.

#

New Publication:
Answers to Common Questions About Sickle Cell Disease

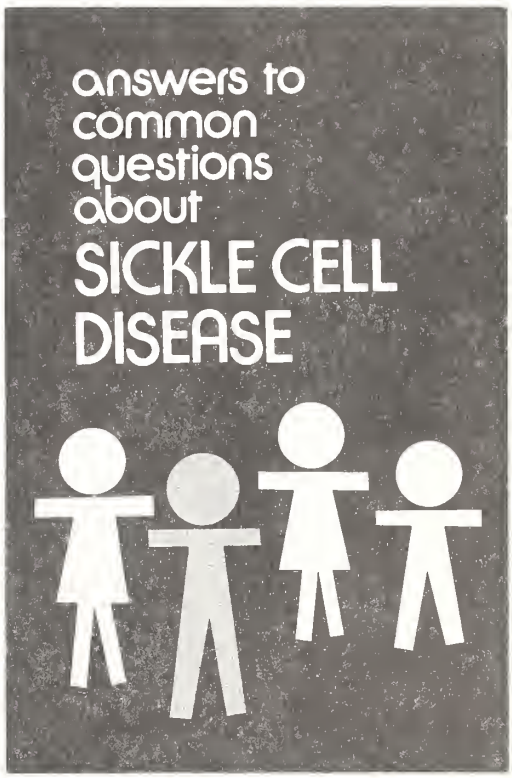
Sickle cell disease, as described in *Answers to Common Questions About Sickle Cell Disease*, denotes all inherited blood conditions in which sickle cell hemoglobin is present, including sickle cell anemia, sickle cell trait, and sickle cell variants. This new pamphlet from the National Heart and Lung Institute (NHLI) explains the differences between the three conditions and documents their likely effects on the carriers and their offspring.

The probability of children inheriting the disease from one or both of their parents is examined in the publication and illustrated in charts. Also, an explanation of why sickle cell disease principally affects blacks is included.

Although there is as yet no cure for sickle cell anemia, this publication furnishes information about research being done throughout the country with drugs to check the harmful effects of the disease. How doctors diagnose sickle cell disease and the importance of testing for the disease is also stressed.

Science writers can obtain a free copy of this publication from:

NHLI Information Office
Landow Bldg., Room C-918
Bethesda, MD 20014
Phone (301) 496-4236



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News Releases Issued

CORONARY SURGERY-- The National Heart and Lung Institute has announced the award of 13 contracts to investigate coronary artery bypass graft surgery. The studies, funded by the Institute's Clinical Cardiac Disease Branch, will include a patient registry and a series of investigations in patients with ischemic heart disease. Participating patients will be carefully selected on the basis of their clinical symptoms and the results of coronary angiography (X-ray visualization of the coronary arteries). Coronary artery bypass graft surgery improves the blood supply to blood-deprived (ischemic) areas of heart muscle and relieves angina pectoris and other clinical manifestations of coronary heart disease.

MINORITY COLLEGES--An additional $1 million for biomedical research at ethnic minority colleges has been added to the Minority Schools Biomedical Support program (MSBS) of the Division of Research Resources. Fourteen new grants were made to institutions not previously supported under the program. The MSBS program now funds 51 grants involving 57 institutions with predominantly ethnic minority student enrollments. The program, designed to strengthen biomedical research activity in minority schools, now involves 45 black institutions, one predominantly American Indian college, one Hawaiian, two Puerto Rican, seven predominantly Mexican-American schools, and one school with large black, Oriental, and Mexican-American enrollments.

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August 25, 1973

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NEWS & FEATURES From NIH August 25, 1973

Research Advances

SURVEY EXPLORES THE LINK BETWEEN "THE PILL," DISEASES

Data gathered in a 24-hospital survey in the greater Boston area sug-test that oral contraceptive use may increase the risk of gallbladder disease in women.

As part of the Boston Collaborative Drug Surveillance Program (BCDSP), investigators screened 5,472 women patients aged 20 to 44 years, in a search for possible associations between oral contraceptive use and gall-bladder disease, venous thromboembolism, and breast tumors.

The BCDSP, a program to study drug effects in large hospital settings, is supported by the National Institute of General Medical Sciences. Findings from the present study are based on reports written by David J. Greenblatt, M.D., (thromboembolism), Howard W. Ory, M.D., (gallbladder disease), and Micha Levy, M.D., (breast tumors), and published in the June 23, 1973 issue of *Lancet*.

According to the investigators, the association between use of "the pill" and gallbladder disease was an unexpected finding. Of the 212 patients with surgically-confirmed gallbladder disease, 65 women (or 31 percent) used oral contraceptives, while the frequency for the 842 controls was 20 percent. At each age level, women using oral contraceptives were at a higher risk of having gallbladder disease. Neither hospital, parity, marital status, nor smoking was related to oral contraceptive use or to gallbladder disease.

(more)

Pill (Cont'd)

Based on these and other statistics, the investigators estimate that "the annual attack-rate of surgically proven gallbladder disease in otherwise healthy women is about 79 per 100,000 in women who do not use oral contraceptives, and about twice that value (158 per 100,000) in those who do."

According to the study findings, the frequency of gallbladder disease in women below the age of 35 years was especially high in those taking oral contraceptives for six to 12 months in comparison to women who took them for longer periods. Despite the fact that most of the older women in the group had taken oral contraceptives for many years, the relative risk of gallbladder disease was higher for users. This suggested to the scientists that oral contraceptives increase the risk of gallbladder disease even after long-term use.

Because gallbladder disease is more common in women of childbearing age than in men, one hypothesis suggested as an explanation for these findings concerns the role of estrogen. Experimental evidence has indicated that estrogen may induce changes in the composition of bile, thus, the "pill's" control of the hormonal balance in a woman's body may potentiate the risk of changing the composition of bile and thus trigger gallbladder disease.

The findings among patients treated for breast tumors and venous thromboembolism proved to be consistent with previously-published reports.

The investigators found a negative association between oral contraceptive use and benign breast tumors. Among the 98 patients with benign

Pill (Cont'd)

breast tumors, six percent (or six women) used oral contraceptives, in comparison with 20 percent of the 842 healthy controls who used "the pill".

Since women with benign breast tumors may have a higher risk of developing a malignancy later in life, "the apparent protective effect of oral contraceptives against benign tumors may also reflect protection against subsequent development of breast cancer," according to the BCDSP scientists.

The investigators also note that statistically, the risk of developing breast cancer is lower for women who become pregnant early in life. Because similarities between "pill" side-effects and pregnancy symptoms may indicate a similar hormonal reaction, oral contraceptive users may in fact be lessening the risk of developing breast cancer.

The authors add, however, that possible long-term effects of oral contraceptives in relation to the risk of breast cancer will have to be evaluated in the future.

In the third research area, the present study indicates that oral contraceptive users are 11 times more susceptible to venous thromboembolism than other women. Their findings confirm the previously reported association between oral contraceptive use and blood clots. The estimated annual attack-rate of venous thromboembolism in women aged 20 to 44 years is six per 100,000, while the frequency for oral contraceptive users is about 66 per 100,000. Among the 43 study women treated for venous thromboembolism, 72 percent (or 31) used oral contraceptives. However, only 20 percent of the control group (170 of our 842) were "pill"-users.

According to the investigators, the estrogen component in most oral contraceptives apparently enhances coagulability and clotting. Virtually all of the oral contraceptive users surveyed took low-dose estrogen preparations.

#

Research Advances

CHIMP ACTS AS KIDNEY MACHINE

Two children in profound coma resulting from liver failure underwent cross circulation of blood with chimpanzees. One patient awoke dramatically five hours after completion of the procedure and remained conscious and alert for 20 days, although significant liver regeneration did not occur.

Researchers from the Duke University Medical Center, the Emory University School of Medicine, and the Yerkes Regional Primate Research Center at Emory, tried this technique on the children after conventional medical therapy had failed. Their work was funded by the National Institute of Arthritis, Metabolism, and Digestive Diseases. Funds for the facilities at the Primate Center are provided by the NIH Division of Research Resources.

The method involved selecting chimpanzees who had no previous clinical illness or infection. The chimpanzees were not anesthesized but received tranquilizers to keep them sedate and were restrained in plaster casts.

Under sterile conditions, doctors inserted plastic tubes into the large vein and artery of the upper leg of the chimpanzee. Simultaneously, they placed identical-sized tubes into the same artery and vein of the patient who was in a coma from liver dysfunction. The researchers began cross circulation of the blood by connecting the arterial and venous tubes from each partner and placing a clamp on each tube to regulate flow.

(more)

Chimp (Cont'd)

In addition to taking constant temperature, pulse, respiration rate, blood pressure, and urine output during the procedure, the doctors performed various clinical studies such as platelet count and blood-urine-nitrogen counts.

In the first case, a three-year-old girl came into the hospital with infectious hepatitis. Her desperate clinical state, characterized by five days of deep coma with abnormal liver and blood function, prompted the decision to institute cross circulation. It was performed for five hours and 50 minutes with no apparent complication.

Despite minor neurological improvement immediately following the treatment, the child remained in a deep coma and died after five days.

In contrast, the five-year-old girl in case two, who also entered the hospital with infectious hepatitis, underwent a longer procedure. In her case, cross circulation lasted for 14 hours and 45 minutes. Five hours after completion the child was conscious, recognized her parents, spoke intelligibly, and answered simple questions. Up until the 20th day she remained alert, although there was no improvement of liver function and her blood would not clot. Generalized bleeding ensued and she died.

The objective of treatment of hepatic coma is to permit survival of patients until their own liver can recover sufficiently to maintain them or they can receive a transplant. Extensive experimenting shows evidence that the liver is capable of reproducing itself after massive sections have been removed. This liver regeneration is especially true in cases of sudden attacks of liver diseases but is less predictable in more generalized disease.

(more)

Chimp (Cont'd)

This is not the first research team to attempt cross circulation between a patient and a healthy nonhuman primate. Other scientists supported a human with hepatic failure by connecting his circulatory system to that of a baboon. In that case, however, the baboon had first been transfused with human blood which cross matched that of the prospective patient.

In the present study, the researchers chose to use the chimpanzee rather than the baboon because it has a closer immunologic identity with man and its distribution of major blood groups more closely resembles those in human beings.

Because preparation for human-primate cross circulation is complex and the performance, although relatively simple, requires numerous people, the research group feels that this method can be used only on people who have not responded to conventional methods and where prognosis warrants further investigative trials.

Other methods of therapy for liver dysfunction might include plasmapheresis, where the blood is removed from the body, washed in a solution, then returned to the body with the plasma removed. It could also be done by extracorporeal liver perfusion, where the person's blood is circulated outside the body through the cleansed liver which has been removed from a healthy animal. The blood is then returned to the patient's body.

According to the researchers, it is hard to establish the superiority of any specific treatment for hepatic coma. In their report, published in the April 1973 issue of *The Journal of Pediatrics*, they state that the small

(more)

number of patients treated with more complex methods does not allow statistical comparison with the traditional regimens. They add that further investigation in providing temporary support for patients with hepatic failure is necessary.

The researchers in this study were H.F. Seigler, M.D., and Richard S. Metzgar, Ph.D., of the Duke University Medical Center, Durham, North Carolina; Robert C. MacDonell, Jr., M.D., Joseph H. Patterson, M.D., Gerald T. Zwiren, M.D., Daniel B. Caplan, M.D., James J. Corrigan, Jr., M.D., James W. Bland, Jr., M.D., Peter A. Ahmann, M.D., and B. Lyn Behrens, M.D., from the Emory University School of Medicine, Atlanta, Georgia.

#

Research Advances

DISCUSSIONS OF FLUORIDE USE HIGHLIGHT DENTAL CONFERENCE

Herschel S. Horowitz, D.D.S., a research scientist with the National Institute of Dental Research (NIDR), believes that self-application may supplant traditional fluoride treatments in the future. Dr. Horowitz presented these findings at the Silver Anniversary celebration of NIDR held in Washington, D.C., on June 28, 1973.

Having children and adults apply fluorides themselves via mouthrinsing, toothbrushing, or mouthpieces may well answer the problems of insufficient professional manpower and funds that currently hinder traditional topical fluoride treatments throughout the world.

Because it is an ideal public health method, fluoridation of community water supplies should be the cornerstone of any national program for preventing tooth decay, according to Dr. Horowitz. He adds that more than 150 million people in approximately 30 countries presently benefit from fluoridated water.

The chief shortcoming of water fluoridation is its limitation to areas with central water systems. A few alternatives--including school fluoridation, use of fluoride tablets, adding fluoride to salt, and the topical application of fluorides--have been suggested to remedy the problem of bringing fluorides to children in geographic areas where it is impossible to fluoridate the water. School water fluoridation programs have been adopted by several states in this country.

At the same meeting, in another discussion of the action of fluoride,

(more)

Fluoride (Cont'd)

Finn Brudevold, D.D.S., of the Forsyth Dental Center, Boston, described ways in which fluoride protects the tooth enamel.

According to the investigator, fluoride is absorbed by the intestine from drinking water and such supplements as pills. This method is most effective when begun at birth and continued until all teeth have erupted because fluoride is readily incorporated into the teeth during their formation.

Dr. Brudevold believes that the chief benefit of fluoride comes from the increased stability it gives to the enamel mineral. He reports finding some correlation between resistance to decay (in terms of cavities and fillings) and the amount of fluoride incorporated in the outer layers of tooth enamel in the same children.

Once teeth have erupted, external applications of fluoride directly to the teeth also help to strengthen enamel. This is particularly true for children's teeth.

Dr. Brudevold also points out that in the first, unnoticeable stage of decay, fluoride appears to combine most readily with enamel; therefore, fluoride treatments at that time may help to remineralize weakened places.

Another possible mechanism of fluoride action is not very well established, according to Dr. Brudevold. Some scientists think that fluoride salts inhibit the metabolic processes of bacteria in the plaque that clings to teeth. However, Dr. Brudevold notes that plaque activity is only slightly and temporarily depressed by fluoride applications. Nevertheless, frequent treatment may give some antibacterial protection.

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Photo Feature

VIRGINIA SCHOOL CHILDREN PARTICIPATE IN FLUORIDE STUDY

The "Swishers and Swallowers" in the Blue Ridge Mountains of Southern Virginia are starting the second year of a dental health study sponsored by the National Institute of Dental Research, at the National Institutes of Health.

(more)

Each week, teachers administer sodium fluoride mouth wash to the "swishers and swallowers" (above). Every day in the school year, the children taking part in the study chew a fluoride tablet, swish the solution through their teeth, and then, on signal from the teacher, swallow the solution (below). NIH is funding this study through the National Institute of Dental Research. (NIH Photos #1110, 1111)

Swishers and Swallowers (Cont'd)

Approximately 1,400 children in the seven Nelson County Schools, under supervision of teachers and dental professionals, are participating in this research project designed to reduce tooth decay.

In addition to the mouth wash and tablet chewing regimen, the children listen to lectures in the school on proper care of the teeth, which emphasize effective toothbrushing and sound dietary practices. Fluoridation is unavailable in the central water system in this area.

The study embraces youngsters in the first six grades and will continue until 1982, with dental examinations every two years.

#

Teachers distribute toothpaste and brushes to children for home use. Parents of the children gave approval of the project, as well as the Nelson County School Board and the Virginia Department of Public Health. This research is funded by the National Institute of Dental Research. (NIH Photo #1112)

News Feature

BASIC RESEARCH NEEDED TO CURB VENEREAL DISEASE

One of the most serious and insidious health problems confronting our country today is venereal disease.

Years ago, it was believed that prostitutes were the primary source of VD. Today, venereal disease has moved from the "red light" districts to the suburbs, invading the high schools and colleges. It attacks people of all races, classes, and ages.

Gonorrhea ranks first among reportable diseases in the United States and is increasing at the frightening rate of 15 percent a year. Infectious syphilis cases in 1972 were three percent higher than in 1971. It has been estimated that the annual incidence of gonorrhea in the United States could well be above 2,500,000 cases a year, with some 80,000 cases of infectious syphilis.

The world-wide increase in venereal disease has been attributed to a number of factors: changing social and moral values, lack of public understanding of what causes VD, non-existence of symptoms, embarrassment at acknowledging exposure to the disease, avoidance of prompt and proper treatment, and under-reporting by physicians of cases they have treated.

Present methods to control gonorrhea and syphilis are expensive. Additionally, they possess features unacceptable to the public and depend largely on treatment after the infection has been recognized.

The Center for Disease Control estimates that one in 50 untreated syphilis victims will develop syphilitic insanity. In addition, one in 25 Americans

(more)

with untreated syphilis will be crippled or incapacitated. These syphilis-related disabilities result in loss of hundreds of millions of dollars in earnings each year, not to mention the loss to the individual of his right to be a self-sufficient, productive member of society.

As researchers expand efforts to treat and control venereal disease, it becomes increasingly apparent that a method to prevent the disease must be found. Such a research program has been mounted by the National Institute of Allergy and Infectious Diseases (NIAID).

Scientists are working with NIAID funds to develop experimental model systems in which to grow VD organisms for studying the infectious processes and for testing diagnostic and preventive measures. Some are investigating the body's immune response--its ability to produce substances which destroy VD organisms. Others are evaluating antibiotic resistance and susceptibility, in an effort to learn more about the underlying mechanism of how antibiotics kill VD organisms.

The answers to many of the questions medical science is asking about gonorrhea and syphilis will not come easily or quickly. The studies require infinite precision and painstaking confirmation. It is true that although a valuable store of knowledge about other bacterial infections can be applied to VD, the problem is that most bacterial infections are not *prevented*--they are *treated*. And, unlike such bacterial infections as a strep throat or pneumonia, the insidious VD organisms often do not produce symptoms.

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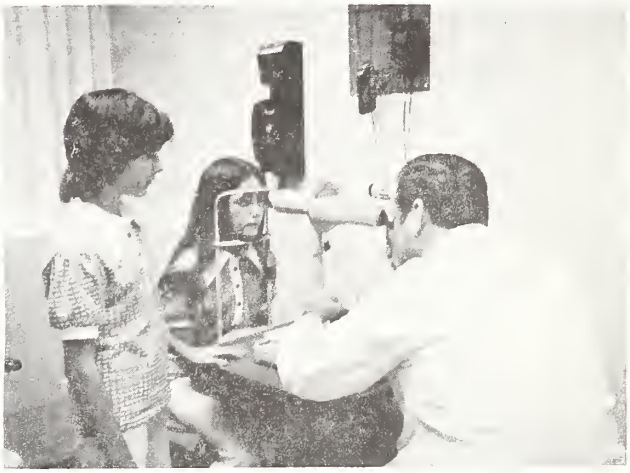
Photo Feature

REGISTER OF 700 PAIRS OF TWINS PROVES USEFUL FOR EYE RESEARCH

"Studies of twins offer interesting and valuable opportunities for genetic and epidemiologic investigations but have found comparatively little use in eye research, particularly in the United States," according to J. Theodore Schwartz, M.D., an ophthalmologist in the National Eye Institute's (NEI) Office of Biometry and Epidemiology.

For approximately 10 years, Dr. Schwartz, Chief of the NEI Section on Ophthalmic Field and Developmental Research, has been involved in ophthalmologic twin studies and has developed a twin register as a resource for his work.

"The purpose in assembling this register," he explains, "was to identify a group of twins who would be readily available for multiple clinical examinations." (more)



J. Theodore Schwartz, M.D., examines identical twins Elizabeth and Anne Marie Riordan for correct muscle balance in the eyes (left photo). In normal vision, both eyes simultaneously direct their gaze at the same object. The two images become fused, and the viewer sees one clear picture. If the eyes fail to do this, double vision results. At right, Dr. Schwartz examines the twins to determine the curvature of the cornea, the transparent membrane at the front of the eye which helps to bend and focus light rays entering the eye. (NIH Photos #1113, 1114)

Twins (Cont'd)

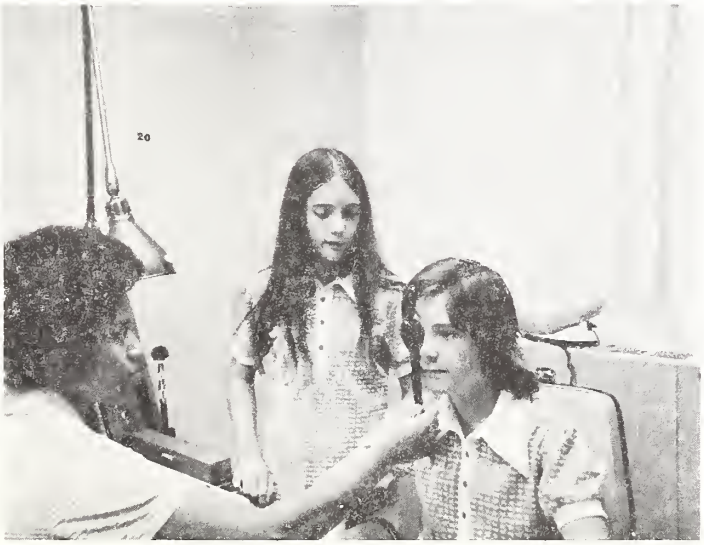
At present there are 700 pairs of twins in the register. About 47 percent of these are identical (monozygotic) twins, assumed to be genetically identical. The fraternal (dizygotic) twins are no more similar genetically than ordinary siblings, but tend to be exposed to a similar cultural and physical environment.

All of the twins in the register are from the Metropolitan Washington, D.C. area. To date, approximately half have undergone a thorough eye examination at the Washington Hospital Center.

In addition to information obtained from the eye examination, the twin register includes medical and perinatal history as well as fingerprints, hand dominance, address, age, birthplace, race, nationality, and family history of each of the pairs of twins. Whether the twins are identical or fraternal, whether they live together, and/or age of separation are also included.

There are several different kinds of twin studies which can be conducted. In the classical twin study, investigators work toward determining the

(more)



Doris Collie, an ophthalmic technician in Dr. Schwartz's office, tests the visual acuity of Anne Marie Riordan. (NIH Photo #1115)

Twins (Cont'd)

relative influence of hereditary and environmental factors on the development of a given trait or disease. In this type of study, a sample of identical twins is compared with a similar sample of fraternal twins.

Dr. Schwartz and his associates recently completed a twin heritability study on the effect of corticosteroids (compounds often used to suppress inflammation) on intraocular pressure. The study, done in collaboration with the National Heart and Lung Institute (NHLI), involved 80 pairs of identical and like-sex fraternal twins who were 15 years of age and older.

The investigation was designed to examine the hypothesis that the rise in intraocular pressure associated with application of topical steroids in certain people is an inherited response. This particular concept has led to a further hypothesis that chronic simple glaucoma, which is associated with elevated intraocular pressure, is an inherited disorder.

(more)

The slit lamp or biomicroscope allows Dr. Schwartz to examine the anterior portion of the eye, especially the cornea. (NIH Photo #1116)

Twins (Cont'd)

However, Dr. Schwartz's study showed a minor role of inheritance associated with the steroid response.

"This new finding is at variance with the widely accepted genetic hypothesis and marks the need for further investigation of the determinants of the steroid response," Dr. Schwartz explains.

Another type of twin study design is the therapeutic trial where physicians offer members of identical twinships having the same disease different treatments in order to compare the relative benefit of the therapies.

Dr. Schwartz is currently conducting such a trial to determine the effectiveness of a treatment aimed at retarding the progression of myopia. Twenty-five pairs of young, identical twins who are similarly myopic are participating in the study. In this investigation, one co-twin receives specially-prescribed bifocal lenses and instills special eye drops in his or her eyes before going to sleep; the other wears conventional eyeglasses as the control.

Dr. Schwartz explained that through the use of identical twins in a therapeutic trial, it is possible to arrive at conclusions with fewer patients because the effect of treatment is likely to be the primary factor influencing the outcome of the study.

Several investigations involving the twin register have also been undertaken in collaboration with the National Institute of Child Health and Human Development, NHLI, and the National Institute of Dental Research.

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Photo Feature

Women in Research...

WOMEN IN TEXAS STUDY GENETICS, REPRODUCTION

Anna Steinberger, Ph.D., is associate professor of Reproductive Biology and Reproductive Endocrinology at the University of Texas Medical School at Houston. At right, she explains the growth of cultured cells to a lab technician. The National Institute of Child Health and Human Development funds her research in defining the factors which control gonadal function in the male. (NIH Photo #1117)

Margery W. Shaw, M.D., professor of Biology, has been at the University of Texas Graduate School of Biomedical Science for five years. Funds from the National Institute of General Medical Sciences have helped her establish a medical genetics center for teaching, research, and services in basic and clinical medical genetics, human population genetics, cancer-related genetics, and interdisciplinary problems in genetics and the law. Dr. Shaw is shown at left obtaining chromosome studies. (NIH Photo #1118)

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NEWS & FEATURES From NIH August 25, 1973

Medical News Tip

VITAMIN DEFICIENCIES IN THE ELDERLY--Investigators in the Gerontology Research Center of the National Institute of Child Health and Human Development are conducting a long-term nutrition survey in a group of more than 600 men. Early results of this study show that with advancing age, there is a reduction in blood levels of thiamine (B1), riboflavin (B2), and pyridoxine (B6)--three vitamins essential to maintaining normal body chemistry.

Two hundred men, volunteers in the Baltimore Longitudinal Study, have been studied to date. Of this group, 30 percent reported taking vitamin supplements. One-fifth of the subjects who were not taking vitamin supplements showed evidence of abnormally low levels of thiamine and riboflavin. Evidence also showed an abnormality in levels of certain enzymes known to change with vitamin deficiency in the plasma and red blood cells.

These results are surprising because the group being studied is comprised of highly educated, community-living subjects who have access to adequate diets. The findings show that nutritional problems exist in advantaged as well as disadvantaged elderly and that vitamin supplementation may be a reasonable means of overcoming deficiencies.

The data is now being examined to determine whether poor nutritional status increases development of age-related diseases, such as arteriosclerosis, diabetes, or hypertension.

For additional information about aging research, contact: Information Office, Gerontology Research Center, Baltimore City Hospitals, Baltimore, MD 21224, Phone (301) 342-5400, Ext. 1401.

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Capsules

FACTUAL FILLERS

ARTHRITIS--Arthritis afflicts about 18 million Americans, reports the National Institutes of Health. Arthritis comes in many varieties with each disorder being a distinct disease form.

RHEUMATOID ARTHRITIS--The most severe form of arthritis is rheumatoid arthritis, according to the National Institutes of Health. This disease damages the ligaments and covering of the joints and muscles.

START DENTAL CARE EARLY--Parents should carefully check the condition of their children's baby teeth, reports the National Institutes of Health. Some of these teeth remain in a child's mouth until the age of 12. If these first teeth are lost, there can be an adverse effect on the spacing of permanent teeth. Also, an infection in baby teeth can damage permanent teeth that are forming in the jaws.

DIABETIC RETINOPATHY--More than 11 percent of Americans who became blind in 1972 lost their sight because of diabetic retinopathy, according to the National Institutes of Health. Diabetic retinopathy is a progressive disorder in the blood vessels of the retina which occurs as a complication of diabetes. Visual impairment associated with the disease results from bleeding into the vitreous, the clear jelly-like substance which fills the center of the eye. Scar tissue then forms and the retina detaches.

Capsules (Cont'd)

MULTIPLE SCLEROSIS--Multiple sclerosis afflicts about 250,000 Americans, according to the National Institutes of Health. It is a major disorder of the central nervous system, affecting many young adults.

VARICOSE VEINS--Varicose veins are widespread throughout the American population and affect almost all ages, reports the National Institutes of Health. They are most common in people over 40, affecting half the women and a quarter of the men beyond that age. With advancing age there is a loss of tone in the skin and tissues that surround and help support veins.

HEADACHE--Headaches can be more than a nuisance, reports the National Institutes of Health; they could be a warning of a serious condition that might be controlled if detected early. People who experience severe or frequent headaches should consult a physician.

RESEARCH HOSPITAL--The Clinical Center of the National Institutes of Health (Bethesda, Maryland) is a 516-bed research hospital. Scientists use the 1,100 laboratories in the hospital to help study patients' diseases.

(more)

Capsules (Cont'd)

RESEARCH ILLUSTRATED

Laboratory animals help National Institutes of Health scientists learn more about life processes. The animals, including these twin monkeys, are well cared for. It is rare for twin monkeys to be born in captivity. (NIH Photo #1119)

This "duck" is not one of the laboratory animals used in National Institutes of Health research. Rather it is a microphotograph depicting a portion of the nucleus of a human cell infected with herpes virus. In the course of the infection the nucleus became distorted. (NIH Photo #1120)

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News Releases Issued

GALLSTONES--The National Institute of Arthritis, Metabolism, and Digestive Diseases has awarded an initial contract for $430,742 to the Cedars-Sinai Medical Center in Los Angeles to supervise and participate in a long-term study of chemical means of dissolving gallstones. The contract-supported study is anticipated to run for five years, involve nine centers, and may ultimately cost more than $7 million. Dissolving gallstones with chemicals may offer a desirable alternative to gallstone related surgery and a possible means of preventing further gallstone development in high risk patients. Such an alternative to expensive surgery, if it proves feasible, would save millions of dollars a year in hospital and related costs.

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September 10, 1973

SPECIAL SUPPLEMENT:
NIH Portfolio on Research on Craniofacial Anomalies

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NEWS & FEATURES From NIH September 10, 1973

Research Advances

SCIENTISTS STUDY METABOLISM OF FLUORIDE IN HUMAN DIETS

Herta Spencer, M.D., working with National Institute of Dental Research support at the Metabolic Research Section of the Veterans Administration Hospital in Hines, Illinois, has recently reported several analytical studies of fluoride (F) in human diets and of fluoride metabolism in adult males.

Although the safety of one part per million of fluoride in drinking water and its efficacy in reducing tooth decay is well established, relatively little is known about the amounts of fluoride in food and its metabolism in humans.

Dr. Spencer measured all the fluoride consumed in food as well as that in drinking water over periods of several weeks, and in some cases over years. She also measured the fluoride excreted in feces and urine (but not that in sweat) as well as monitored plasma fluoride at various times. Most of these studies were based on food and water in the Chicago area, but one study covered diets in 15 cities from New York to California and from Alabama to Wisconsin. Another study dealt with baby foods purchased in the Chicago area, but processed in various places. None of the concentrations of fluoride produced any signs of toxicity, and they varied over a considerable range.

The baby foods had a surprising amount of variation. For example, the milk substitute, similac, contained 0.3 mg fluoride per liter in its ready-to-use form, whereas the similac concentrate had three times as much fluoride. Dilution of the concentrate with an equal amount of Chicago fluoridated tap water also gave the baby 0.9 mg fluoride per liter, but mixed with distilled

(more)

water (one-to-one), it delivered only half as much fluoride to the baby. Baby apple juice varied from 0.74 to 1.5 mg fluoride per liter and baby chicken ranged from 1.5 to 3.0 mg F/kg, containing five to ten times more fluoride than beef and pork which varied only from 0.3 to 0.4 mg F/kg.

Dr. Spencer noticed that daily, dietary intake of fluoride (calculated according to pediatrician-recommended amounts of food and excluding drinking water which is negligible for the very young child) averaged about 0.4 mg per day for the first two months, and doubled for children three to six months of age. On the average, a 15 lb. infant of about six months would consume 0.053 mg F per pound per day, whereas a 170 lb. man averaging 4.0 mg F intake per day, would consume only 0.029 F per pound per day.

In Chicago, Dr. Spencer found that a range of 1.4 to 2.0 mg F per day of a man's daily intake of 4.0 to 4.5 mg F came from food and the rest from drinking water. However, in the study of 15 cities, the fluoride content of men's diets sometimes varied by a factor of two, and that of their drinking water varied even more. Even when the water content differed by only 0.29 mg as between Milwaukee (1.14) and Louisville, Kentucky (0.85), the total daily intake was 3.41 mg F in the former compared to 1.98 mg F in the latter largely because the Milwaukee breakfast contained three times as much fluoride as the Louisville one.

Diets high in fluoride found in areas with little fluoride in the drinking water are traceable to foods processed in high fluoride areas and to differences in the types of foods. About 50 diets a year (exclusive of drinking water) measured in Chicago from 1967 through 1972 showed a daily average

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range per year that varied from 1.6 mg F to 1.9 mg F. Fluoridation of Chicago water added about twice as much fluoride to each meal as was found before.

Dr. Spencer's metabolic studies showed that about half of each day's consumption of fluoride is normally excreted in the urine, and about six percent in the feces. The remainder, an average 1.5 mg F/day, is largely retained. When large doses of sodium fluoride which have a very high fluoride content were given for treatment of osteoporosis to supplement human intake to approximately 40.0 mg/day, about 60 percent was excreted in the urine and 11 percent in the feces. Plasma levels of fluoride reach a maximum of two or three times the fasting level 30-60 minutes after intake, and decrease gradually thereafter. Salivary fluoride mirrors the levels of ionic fluoride in plasma.

When Dr. Spencer tested the effects on fluoride metabolism of adding three levels of calcium (223, 1371, and 2135 mg/day) and two levels of phosphorus (800 and 1400 mg/day) to the diet, she found that these minerals neither singly nor together affected the urinary output of fluoride. The fecal fluoride averaged 0.28 mg/day with the lowest calcium supplement, with or without the extra phosphorus.

However, fecal fluoride increased similarly when phosphorus was added to both intermediate and high calcium supplements, and more than it did when calcium was given alone. Apparently the added minerals have the same effect whether the fluoride intake is 4.4 or 13.8 mg/day. The overall fluoride balances changed but little. When calcium was given intravenously, less

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fluoride was excreted in the urine, so the retention of fluoride seems to be associated with retention of calcium and phosphorus. Magnesium given by mouth caused a variable increase in fecal excretion of fluoride.

Plasma levels of fluoride remain quite constant at all hours of the day for months at a time during periods of low fluoride intake, according to Dr. Spencer. After single doses of 10-20 mg F, the plasma level rose sharply for an hour but usually returned to the base line in 24 hours. When a dose of 20 mg F/day was given daily for three months, the fasting levels just before administration of the next dose remained the same, but when 50 mg F/day was given for three months, the daily fasting level increased after a few days then leveled off, and decreased promptly to the pretreatment level after treatment stopped.

Dr. Spencer and her associates reported much of this dietary analysis at the International Association for Dental Research meeting in Washington, D.C. in April, 1973. Some information on "Fluoride Metabolism in Man" was presented at the Seventh Annual Conference on Trace Substances in Environmental Health at Columbia, Missouri, June 12, 1973, and other data on the "Effect of Different Ions on Fluoride Metabolism in Man" were given at the Second International Symposium on Trace Element Metabolism in Animals at Madison, Wisconsin, June 18-23, 1973.

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Research Advances

NEI SPONSORS CONFERENCE ON VISUAL PIGMENT RESEARCH

To further interest in visual pigment studies, the National Eye Institute (NEI) sponsored a conference in June 1973 on the status of research on rhodopsin, its chemistry and function. Rhodopsin is the light-sensitive pigment found in the membrane of the rod-shaped photoreceptor cells of the retina.

Composed of a vitamin A derivative (retinal) and a protein group (opsin), rhodopsin separates into these two components when "bleached" by light, but regenerates in the dark. This unique property is responsible for the retina's ability to adapt to varying degrees of light. It is also a key step in the transformation of light energy into visual perception. Better understanding of rhodopsin and its place in visual excitation is the goal of many studies in the visual sciences and is one of the most important areas of basic research related to disorders of the eye and visual system. The field has attracted the attention of many new investigators and in recent years new insight into the nature of rhodopsin has resulted from new approaches taken in the study of this visual pigment.

About 30 scientists representing various aspects of visual pigment studies presented papers at the rhodopsin conference. They discussed the chemical properties of rhodopsin, its location within the discs which make up the rod cell outer segments, its mode of synthesis, and the role of rhodopsin in the visual process.

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Rhodopsin (Cont'd)

The chemical events that follow the bleaching of rhodopsin are of great interest. A major question is how a single photon of light could be strong enough to power the chemical and electrical system that produces vision. Attempting to answer this question, scientists have postulated that a chemical transmitter (or transmitters) may be involved in the amplification of a light-triggered signal. Increased attention has been given to the possible role of calcium in such a mechanism. It has been found that calcium may affect the permeability of the rod disc membrane and block the flow of sodium ions, thus altering the electrical potential of the membrane.

Because rhodopsin is exclusively located in the rod disc membrane, the precise structure of the rod outer segment discs is another important question. X-ray diffraction studies presented at the conference seem to indicate that rhodopsin is located inside the disc on the inner disc membrane. Other studies suggest that rhodopsin is bound on the outer surface of the disc. To reconcile these findings, it has been suggested that the rhodopsin molecule is shaped as an elongated oval which penetrates through the disc. Through a process known as freeze etching, one investigator has shown electron microscopic pictures indicating that a rhodopsin-like molecule is present in the disc in just such a conformation. Another explanation is that the molecule is composed of two distinct structures: an electron-dense globe which would be visible through X-ray diffraction and a tail structure which penetrates the outer disc. It is also worthy of note that rhodopsin apparently can move freely within the disc membrane.

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Rhodopsin (Cont'd)

Investigators have also directed attention to adenylate cyclase in the photoreceptor membranes. This enzyme converts adenosine triphosphate (ATP) to adenosine cyclic monophosphate (cyclic AMP) and exists in virtually every animal tissue. In each tissue, the cyclase system appears to regulate whatever physiologic function takes place and serves as a kind of intracellular communications system. Discovery of a light-sensitive adenyl cyclase in the rod cell outer segment membrane has stimulated research to determine what role, if any, this enzyme plays in the conversion of light energy to electrical impulses.

Although a number of investigators think that the adenyl cyclase system probably plays a major role through cyclic AMP in regulating permeability of rod membranes, leading to the modulation of the electrical potential of the membrane, direct evidence of this has yet to be presented.

Other rhodopsin studies are examining the role of polyunsaturated fatty acids in the visual cell. Animal experiments suggest that these substances are essential for normal turnover of discs. Other investigators are working on the biosynthesis of rhodopsin in vitro or the biosynthesis of disc membranes in vivo using radio-labelled compounds.

The three-day rhodopsin conference was coordinated by Hitoshi Shichi, Ph.D., of the NEI Laboratory of Vision Research. Other NEI participants were Jin Kinoshita, Ph.D., Chief, Laboratory of Vision Research; Marc S. Lewis, Ph.D. Paul J. O'Brien, Ph.D., and Shuko Yoshikami, Ph.D., Laboratory of Vision Research; and Robert N. Frank, M.D., Clinical Branch.

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Rhodopsin (Cont'd)

Other NIH participants were Ralph G. Adams, Ph.D., Laboratory of Chemical Physics, and William Hagins, Ph.D., Laboratory of Physical Biology, National Institute of Arthritis, Metabolism, and Digestive Diseases. Nobelist George Wald, Ph.D., was also among the conference participants and made concluding remarks concerning his impressions regarding the new developments in rhodopsin research.

Papers presented at the NIH rhodopsin conference are scheduled for publication in a special issue of the journal *Experimental Eye Research*.

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Research Advances

BONE TRANSPLANTS OFFER HOPE TO CANCER, ACCIDENT VICTIMS

Those victims of war, accidents, birth defects, and cancer surgery who need facial bone are now being helped with transplants of their own marrow and cancellous (inner, porous) bone.

Philip J. Boyne, DMD, reported on several new procedures which stimulate formation of new bone at the 25th Anniversary celebration of the National Institute of Dental Research, held in June 1973 in Washington, D.C.

Dr. Boyne, of the University of California at Los Angeles School of Dentistry, described bone transplant procedures that have been used to treat Vietnam war casualties with jaw defects. A needle is used to remove marrow and bone without an incision except when larger amounts are needed to repair larger jaw areas. Then, tissues are placed into a metal trough lined with a special filter, and the trough is implanted where new bone is needed.

When large sections of bone are needed to replace an entire jaw bone, the marrow and cancellous grafts must be supplemented. According to Dr. Boyne, the best type of supplementing transplant to use appears to be surface-decalcified cancellous bone taken from another individual.

The same system has also been used successfully in children with cleft palates (an opening in the roof of the mouth). Although surgery to repair the birth defect generally is performed during infancy, sometimes the cleft cannot be closed completely. Rib grafts to fill the space had been tried without success. In contrast, marrow and bone grafts function so well that they withstand the tremendous forces of chewing and orthodontic treatment.

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Transplants (Cont'd)

Although teeth have been transplanted from one person to another since ancient times, they still do not last more than an average of four years, Dr. Boyne explained. To date, the most successful type of transplant involves the use of an immature wisdom tooth to replace a missing tooth in the same person. Even a tooth reimplanted into its own socket can fail to endure if the tooth is fully mature or if it has been out of the mouth too long.

Therefore, man-made products are being tested for tooth implants. Metal implants buried below the tooth-supporting alveolar ridge used with bone grafts are being tested in people whose ridges have wasted away leaving too little bone to support dentures. Promising tests in monkeys have led to human trials which "promise improved dental function for patients who have no alternative to conventional dentures," Dr. Boyne said. He added that such implants "have opened a whole new area of possible improvement in health care."

Dr. Boyne formerly served at the National Naval Medical Center in Bethesda, Maryland.

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Photo Feature

92% of Body Burned...

GIRL SURVIVES BURN ACCIDENT

An eight-year-old girl will live despite "as large a burn injury as a human being has ever survived," Charles Baxter, M.D., professor of surgery at the University of Texas Southwestern Medical School, recently announced. The girl was burned over 92 percent of her body in an accident in her home on May 10 of this year.

Dr. Baxter, whose burn research is funded by the National Heart and Lung Institute, attributed this survival to the latest techniques in burn therapy and the establishment of the new Dallas Skin Bank which provided the needed human skin for grafting.

(more)

Sherry White is hospitalized in the controlled environment of the Parkland Hospital Pediatric Burn Unit, Dallas, Texas. (NIH Photo #1121)

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Burn (Cont'd)

Sherry White, daughter of Mr. and Mrs. William White of Dallas, was injured when the gasoline being used to clean tar from her feet ignited. She received second and third degree burns on her entire body except the sole of her right foot and the back of her head where hair grew.

Most patients who have received burns over 50 percent of the body have died. Dr. Baxter said that a combination of techniques including new concepts in nutrition, new ways of administering antibiotics, isolation, monitoring of tissue for bacteria, use of human skin as protection, and early surgical removal of burn tissue contribute to the medical victory of this little girl.

One of the main reasons for Sherry's survival was use of human skin from the six-month old Dallas Skin Bank. The bank is both a repository for human skin kept viable by freezing and a research center for developing some of the new techniques which were used with Sherry.

Human skin may be used for grafting immediately or frozen

Dr. Baxter adds a bit of motivation by "betting" Sherry a dollar for each hard task she performs. Here she walks with the nurse. (NIH Photo #1122)

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for later use if it is removed from the donor less than 24 hours after death.

Because Sherry's mother was the only living donor, skin from the bank was matched by blood and tissue typing techniques. The graft which the doctors used to cover Sherry's exposed wounds will keep infection from spreading and help regenerate the growth of her skin. She will eventually reject the foreign skin, but this will happen gradually.

Another new technique used on Sherry was early massive excision of the burned tissue. The cutting away of the burns has traditionally been done at a later time.

Nutrition plays an important role in the survival of a burn patient since so many calories are lost when the body loses its protective covering and energy escapes. The doctors gave Sherry special nutrients with intravenous drip, nose tube, and oral feeding.

Infection in an open wound could result in death for a burn patient. Dr. Baxter and William Curreri, M.D., assistant professor of surgery, developed a new biopsy technique to monitor the level of infection in the wound. They take tissue from the wound and do cultures which enable them to be aware of dangers much sooner than has been possible previously. They can start antibiotic treatment immediately at any warning sign.

Dr. Baxter said another life-saving technique developed at the Dallas medical school is sub-eschar clysis, the administration of antibiotics between live tissue and dead burn tissue. When a new infection starts, the topical application of antibiotics to the explicit area is added to more traditional methods.

(more)

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Burn (Cont'd)

According to Drs. Baxter and Curreri, the school researchers in the Burn Center are particularly involved in studying the most optimal antibiotics as well as nutritional combinations.

Nutrition plays a big part in the survival of a burn patient since 2 1/2 to 3 times the normal intake of calories is necessary. Since Sherry requires 3,700 calories per day, her mother brings in her favorite foods such as tacos, spaghetti, and even pizza (left). At right, Sherry plays with Charley, the dog that Dr. Baxter gave her. The dog is freshly bathed and wrapped in a baby blanket on his occasional visits. The company is important for Sherry because she will spend another month at Parkland Hospital Pediatric Burn Unit before being transferred to another hospital for plastic surgery. Funds for Dr. Baxter and his associates in research are provided by the National Heart and Lung Institute. (NIH Photos #1123, 1124)

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NEWS & FEATURES From NIH September 10, 1973

News Feature

ASBESTOS-RELATED DISEASE "EPIDEMIC" OFFERS CHALLENGE TO MEDICAL RESEARCH

One of the critical problems facing Americans is how to live productively and safely in a society in which new hazards seem to develop every day.

Our highly developed and imaginative chemical industry develops thousands of new compounds each year, of which approximately 300 are incorporated into products that we all use. The safety of most of these compounds is unknown. Even less well known is the extent to which they may combine with compounds already in our environment to create new hazards. This reason prompted the "Toxic Substances Control Act," which will require all new compounds to be adequately tested before they come into general use.

An unsolved problem facing Americans is how to protect themselves from hazards associated with compounds they are using, many of which seem essential to everyday living and to continued economic development. Nowhere is this dilemma more sharply apparent than in the case of asbestos.

Perhaps no other mineral is much a part of American life as asbestos. Impervious to heat, asbestos fibers are fashioned into fireproof clothing and theatre curtains, and such common household items as noncombustible drapes, rugs, pot holders, and ironing board covers. Mixed into slurry, asbestos is sprayed onto girders and walls to provide new buildings with fireproof insulation. It is used in floor tiles, roofing felts, in most plasterboards and wallboards, plaster and stucco, and many paints and putties.

(more)

Asbestos (Cont'd)

This "mineral of a thousand uses," is probably present in some form in every home, school, office building, and factory. Used in brake linings and clutch facings, in mufflers and gaskets, and in sealants and caulking, asbestos is also a component of every modern vehicle, including spacecraft.

At first regarded as relatively harmless to man, asbestos has gradually come to be recognized as the probable cause of asbestosis, a fine scarring in the lungs of persons long exposed to its dusts. In the late 1950's, asbestos also was suggested as the probable cause of a peculiar form of cancer called mesothelioma, which up to that time had been a textbook rarity.

Later studies confirmed its role in both diseases and as a cause of the more common type of lung cancer as well. In cigarette smokers exposed to asbestos it is particularly deadly.

An estimated five million American men and women--workers in asbestos plants, insulation workers, construction workers, steamfitters, carpenters, tile setters, and others--daily breathe in significant amounts of asbestos fibers. An estimated 40 percent of these workers who are heavily and directly exposed to asbestos will die as a result of the exposure. It is not yet known with certainty whether mesothelioma or other cancers result only from heavy exposure or whether prolonged low-level exposure will be equally injurious.

Shipyard workers in the British Isles who were building ships in the mid-1930's are only now being stricken with mesothelioma. This increased incidence, first reported in about 1970, thus is being discovered 35 years after the exposure.

(more)

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Asbestos (Cont'd)

In this country, ship building intensified in 1940 and continued as we became involved in World War II. Approximately 2 1/2 million American workers were exposed to asbestos as were their colleagues in Europe. It must be assumed that they also are now at risk of developing mesothelioma.

The asbestos hazard would be serious enough if the workers were the only group at risk, but the problem extends further. Asbestos fibers can be found in the lungs of every adult who lives in large urban areas such as New York City, because in many buildings the air supply is contaminated as it passes through asbestos-lined spaces. Since little is known of the effects of such prolonged low-level exposure, there is cause for concern about these large populations.

The failure to research the asbestos problem in the 1930's and 1940's has left us with a terrible legacy. We knew in the 1930's that asbestos can cause some scarring of the lungs when it is inhaled, but, because the significance of this was not realized, we used asbestos rather freely and with few precautions. Now we can expect an epidemic of asbestos-related diseases. Retrospective recognition of this environmental health hazard has stimulated long-term research such as that undertaken and supported by the National Institute of Environmental Health Sciences (NIEHS).

Approximately seven years ago, the NIEHS began to support rather extensive research on asbestos. As a result, scientists now know the consequences of uncontrolled industrial use of the material. Remaining, however, is the critical task of finding ways of inactivating the dust already fixed in our bodies. There is an urgent need for us to find substances which can

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Asbestos (Cont'd)

alter the dusts already deposited in human lungs and prevent otherwise inevitable disease.

In 1973, NIEHS began supporting an Environmental Health Sciences Center which concentrates on asbestos research. This Center has been established at Mount Sinai School of Medicine, under the direction of Irving J. Selikoff, M.D., a pioneer in asbestos epidemiology.

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Photo Feature

Women in Research...

FLORIDA SCIENTISTS STUDY AMOEBA, PARASITES

The National Institute of Allergy and Infectious Diseases (NIAID) is providing funds for research by Catherine A. Crandall, Ph.D. (left), of the University of Florida College of Medicine, who is shown using a cytocentrifuge to make slide preparations of cells. Her study is focused on quantitating immunoglobulin-containing cells in the lymphoid tissues of animals which are infected with parasites. The parasites used in the study are implicated in such human infectious diseases as trichinella and ascaris. Ascaris (intestinal worms) is especially common in poverty-striken areas of the South. Dr. Crandall has been at the University of Florida in Gainesville for 12 years. (NIH Photo #1125)

Ann Stevens Larkin, Ph.D., (right), is sampling a culture for growth of particular disease-producing amoeba, acanthamoeba, which is a causative agent in human encephalitis, or inflammation of the brain. Dr. Larkin, who has been at the University of Florida College of Medicine for 4 1/2 years, is also funded by NIAID. (NIH Photo #1126)

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Photo Feature

ROCHESTER MENTAL HEALTH PROJECT HELPS PREVENT STUDENT FAILURE

There may yet be a brighter future for youngsters who cannot adapt to school and who are not getting the education they will need to cope with life.

Help is on the way through a project the University of Rochester started in 1958 with the cooperation of local school districts. Ways have been found to detect and treat school maladaptation from the very beginning of the child's school years.

The model is now being adopted in several States throughout the country.

The Rochester project has a simple principle: "Grab the problem early and help the child overcome it, before it takes hold and handicaps him for the rest of his life." The goal is to help school children reach the educational and adjustment level that is equal to their aptitudes and abilities. The project has been so successful that teams of school administrators, educators, school aides, psychologists, psychiatrists, social workers, and others from throughout the country now are going to Rochester for short courses in how it is done.

The program, called the Primary Mental Health Project (PMHP), was launched in Rochester by Emory L. Cowen, Ph.D., of the University's Psychology Department to solve city and county educational problems. Funding was in part from the State Department of Mental Hygiene and school districts from 1958 to 1963. Research, training, and services were combined in an effort to meet what was seen as a growing failure in American education. Dr. Cowen had the idea (since confirmed by statistical studies) that about 30 percent of

(more)

the children in school had adjustment problems--often lasting and severe--and that 10 percent needed immediate professional help. He believed that in some urban poverty areas, school maladaptation might approach a far higher figure.

HEW's National Institute of Mental Health began funding in February 1969, and in all has made $380,000 available for the PMHP. Support also now is coming from local and voluntary agencies and individuals. Federal and other funding has enabled Dr. Cowen to expand the work in Rochester and Monroe County. He also has begun a series of training courses for school personnel from other parts of the country, which has made it possible for them to launch satellite programs in their own school districts. In consequence, projects are continuing or pending in Michigan, Connecticut, Virginia, Iowa, and Texas, all but one of which will be under local funding.

One phase of Dr. Cowen's approach has been based on the belief that school failures cause young children to develop emotional problems because of a resulting poor self-concept, sense of inadequacy, shame, ridicule from others, and similar factors--rather than that they enter school with emotional problems which cause them to fail.

The PMHP takes into account the ways emotions can affect learning, the influence of the school milieu, the effect of family relationships and dynamics on adjustment, the fact that early school maladaptation may continue into adulthood if early treatment is not available, and finally, the fact that treatment is more effective and more economical if begun early.

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School Project (Cont'd)

Not everyone can take the week-long intensive workshops offered at Rochester. Those accepted for the courses must be of proven leadership in their own school districts, have backing to start a similar project at home, and be working "on the firing line," that is, in areas where help is needed and can be utilized.

In 1973-74, Dr. Cowen will conduct another study course for teachers, administrators, and aides, and will invite the participants back later to spend a month as interns, learning the day-to-day operation of the project. Consultation visits from PMHP staff will be made available to help launch the satellite projects.

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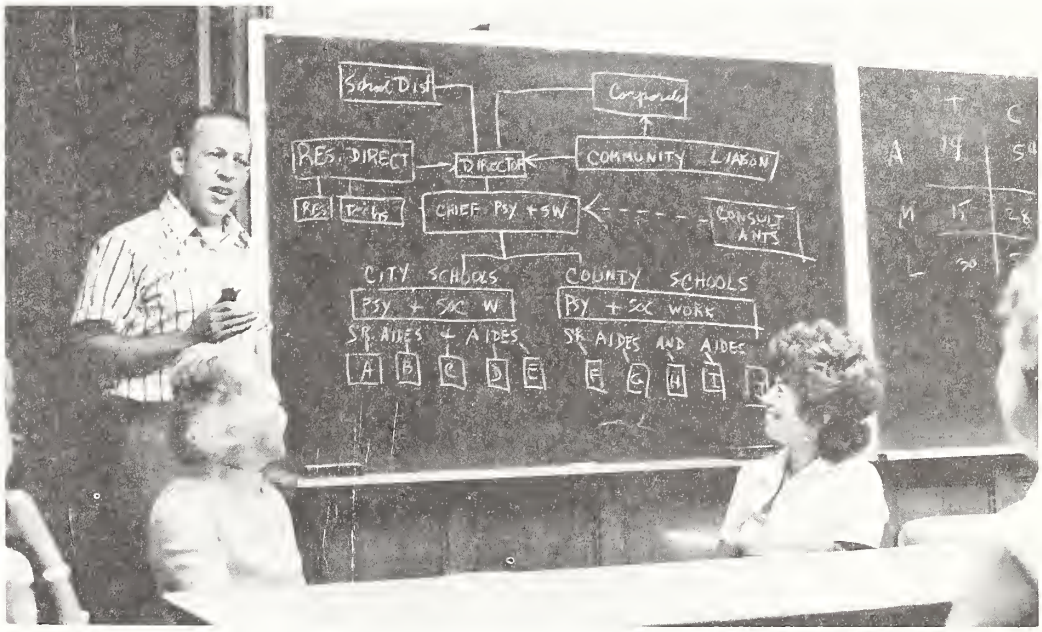

Using a mixture of school-based mental health professionals, non-professional child-aides, and substitute teachers, the Primary Mental Health Project brings school mental health services to more than 7,000 primary graders in 13 schools. (NIH Photo #1127)

Medical News Tip

MALNUTRITION IN THE U.S.--Until recently, severe malnutrition in children was thought to exist only beyond the borders of the United States. An NIH-supported comprehensive survey of the nutritional status of the lowest economic quarter of the U.S. population has bared some facts that may startle many Americans.

The study indicates that many children in this country suffer from kwashiorkor and marasmus, diseases usually associated with poverty in the developing nations. Kwashiorkor, a condition resulting from chronic lack of protein, results in severe growth retardation, vulnerability to illness, swelling of the abdomen with water, and marked apathy. Marasmus, a disease marked by wasting, emaciation, and starvation of body tissues, is caused by extreme calorie deprivation.

Because low-income American mothers seldom breast feed, their children are often denied the initial period of near-normal growth enjoyed by children nursed by mothers in even the poorest of countries. The milk of a poorly nourished nursing mother, although often deficient in volume and vitamin supply, can provide an infant with the basic nutrients required in his very early growth period.

For further information about research in this area, contact:

Information Office
Division of Research Resources
Bldg. 31, Room 5B-39
NIH, Bethesda, MD 20014
Phone (301) 496-5545

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ARCHIVE

Capsules

Factual Fillers

DIABETIC RETINOPATHY--Diabetic retinopathy, a disorder of the blood vessels in the retina stemming from diabetes, is a leading cause of blindness in this country according to the National Institutes of Health. The retina is the innermost layer of the eye, composed of sensitive nerve fibers which are connected by the optic nerve to the brain.

RETINITIS PIGMENTOSA--Retinitis pigmentosa is an inherited eye disease that usually produces its first symptom--night blindness--in children or adolescents. Over a lifetime, the disease gradually decreases a person's ability to see at night and cuts down on the amount of side vision, resulting in "tunnel vision," according to the National Institutes of Health.

CORNEAL DISEASE--Diseases of the cornea, the transparent membrane at the front of the eye which helps to bend and focus light rays, are often the most painful of eye disorders, according to the National Institutes of Health.

LYMPHOMAS--The major lymphomas are Hodgkin's disease, lymphosarcoma, and reticulum cell sarcoma. Lymphomas are characterized by abnormal growth of cells making up the lymphatic tissue; they differ as to which cells are affected, according to the National Institutes of Health.

ACUTE LEUKEMIA--Acute leukemia in children usually appears suddenly with symptoms similar to those of a cold, and progresses rapidly. The lymph nodes, spleen, and liver may become infiltrated with white blood cells and enlarged,

(more)

and there may be bone pain, paleness, tendency to bleed or bruise easily, and frequent infections, according to the National Institutes of Health.

CHRONIC LEUKEMIA--Chronic leukemia, the most common form of the disease in adults, comes on slowly and without warning. Many cases are discovered during routine examinations and, even after changes in the blood are noticed, several years may pass before significant symptoms appear, according to the National Institutes of Health.

STROKE RISK--The person known to have a greater than average risk of a stroke probably has one or more of these problems: overweight, a diet high in fats, high blood pressure, smoking. He may have atherosclerosis, heart disease, diabetes, or other ailments already diagnosed or as yet unknown to him, according to the National Institutes of Health.

HEART ATTACKS--During a heart attack, the damaged heart muscle signals the degree of its distress by releasing enzymes into the blood stream. The chemical measurement of these enzymes is most useful in determining recent heart injury, according to the National Institutes of Health.

(more)

Capsules (Cont'd)

RESEARCH ILLUSTRATED

These scanning electron micrographs provide close looks at two substances under study by NIH grantee scientists. At right are Ambrosia ragweed pollen grains magnified 3,000 times. Below is dental amalgam. The pollen was photographed at Harvard University, while the amalgam was photographed at the University of Virginia. (NIH Photos #1128, 1129)

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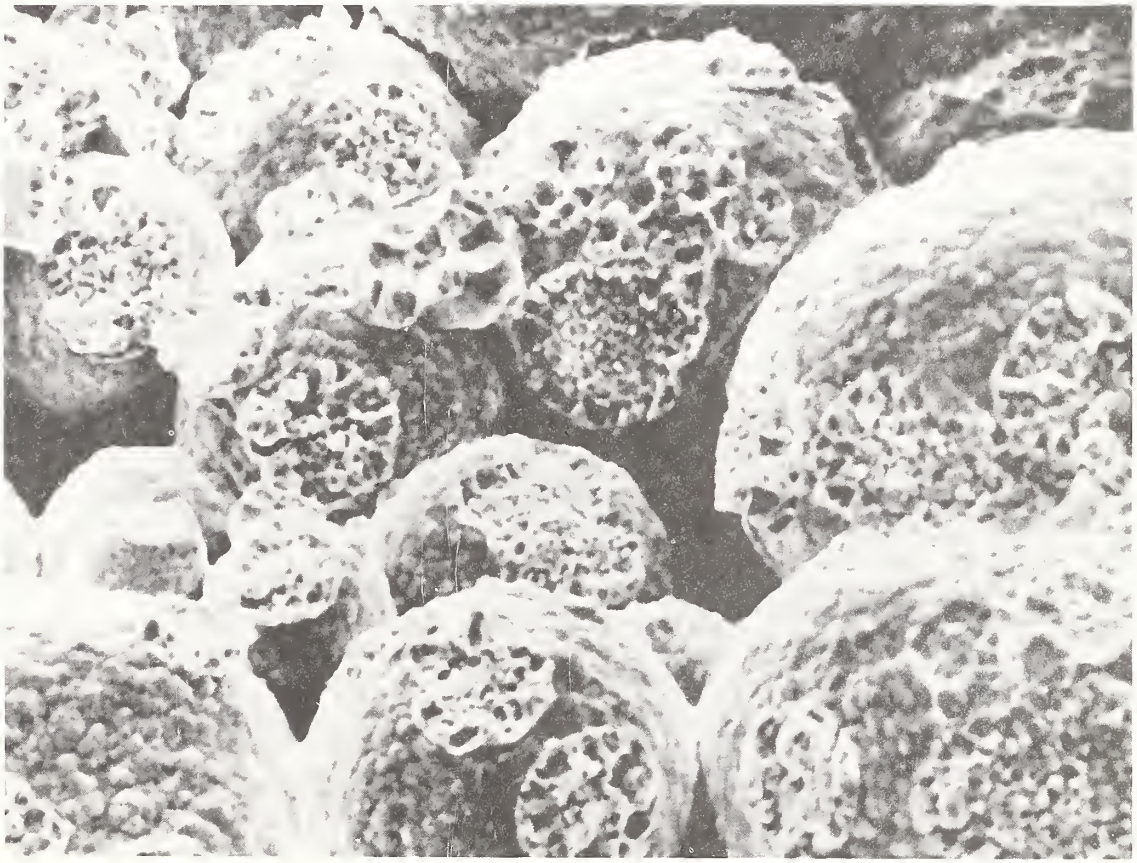

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NEWS & FEATURES From NIH
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NEWS&FEATURES FROM NIH

PORTFOLIO - RESEARCH ON CRANIOFACIAL ANOMALIES

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE ■ Public Health Service ■ National Institutes of Health ■ Office of Information ■ Bethesda, Maryland 20014

September 1973

NEWS&FEATURES FROM NIH

THE NIH PORTFOLIO ON RESEARCH ON CRANIOFACIAL ANOMALIES....SEPTEMBER 1973

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE ▪ Public Health Service ▪ National Institutes of Health ▪ Office of Information ▪ Bethesda, Maryland 20014

Marc Stern, Editor --- Carol M. Sussman, Associate Editor

NIH News Branch, Building 31, Room 2B-10, Bethesda, MD 20014, [301] 496-1206

INTRODUCTION: NIDR STUDIES MAJOR ORAL, CRANIOFACIAL MALFORMATIONS

This Introduction was prepared with the assistance of Richard L. Christiansen, D.D.S., M.S.D., Ph.D. Dr. Christiansen is Chief, Extramural Craniofacial Anomalies Program, National Institute of Dental Research (NIDR). NIDR is a component of the National Institutes of Health, an agency of the U.S. Department of Health, Education, and Welfare.

Oral-facial disfigurement and dysfunction are among the most handicapping of all human ills. Mechanization has reduced the impact of many types of physical disabilities, but the special problems of those with malformations of the head and face remain undiminished. In fact, as the need for personal interaction and communication increases in our society, these problems become intensified.

Oral and craniofacial malformations constitute an important area of study of the National Institute of Dental Research (NIDR), a component of the National Institutes of Health. Major emphasis is on congenital malformations, such as clefts of lip and palate, and malocclusion of teeth and jaws. Carried out largely through grant support, these studies have their principal focus in the Craniofacial Anomalies Program in NIDR's extramural programs.

(more)

Dento-facial malocclusion is very common, affecting at least three-quarters of the population of the United States in some degree. In about one-third of the people, the malformation is sufficiently severe to require treatment. Studies supported by NIDR include efforts to determine how growth of jaw and other facial bones may be influenced or controlled, in the hope of eventually intercepting or preventing some forms of malocclusion at very young ages.

The most common congenital craniofacial anomalies, clefts of lip and palate, cause severe deformity and impairment of such functions as mastication, swallowing, and speech. Clefts occur about once in every 700 births, affecting 6,000 to 7,000 newborn babies each year. They constitute 13 percent of all reported birth anomalies.

For more than a decade, NIDR has been the chief source of support for research to improve the management, treatment, and psychosocial adjustment of children with clefts. Because of this research support, dramatic progress has been made in improved diagnostic, surgical, dental, and speech techniques to restore afflicted children to near-normal appearance and function.

NIDR has sponsored the development of the team approach to cleft treatment. Pediatricians, surgeons, orthodontists, prosthodontists, speech pathologists, and others with specialized training coordinate their efforts to study and treat the "total" person. Psychological studies are contributing insights to the problem of total habilitation after anatomical and functional repair.

Attention is also being directed to etiologic factors. It is still not clear what specific events occur in embryonic life to produce the cleft lesion. Some clefts appear to have an hereditary basis. However, the interactions of genetic and environmental factors are still not understood.

Significant strides have been made toward greater understanding of normal as well as abnormal craniofacial growth, maturation, and aging. Efforts in this regard have been productive in accumulating vast pools of data on samples of normal human populations, including distinct ethnic groups.

While continuing its studies on clefts and malocclusion, NIDR is enlarging the compass of its research to include other craniofacial anomalies. Less common but frequently more disfiguring congenital craniofacial malformations are now under study. These include severe jaw malformations, ear deformities, eyes which are excessively set apart and prevent normal vision, and a cranium with sutures that do not grow, thus causing damage to the growing brain and a distortion of the facial structures. Usually, the anomaly includes a combination of these deformities and perhaps malformations of other parts of the body, such as feet and hands.

"There are many thousands of facially disfigured people--victims of birth defects--who remain isolated from society, confined to mental or other institutions, or isolated at home, who must now be given an opportunity for a more normal life," according to Seymour J. Kreshover, D.D.S., M.D., Ph.D., NIDR Director. "These people have been hidden from society because basic methods of treatment were not available. There is now hope through research for innovative surgical procedures to help these forgotten people."

List of Scientists Studying Craniofacial Anomalies

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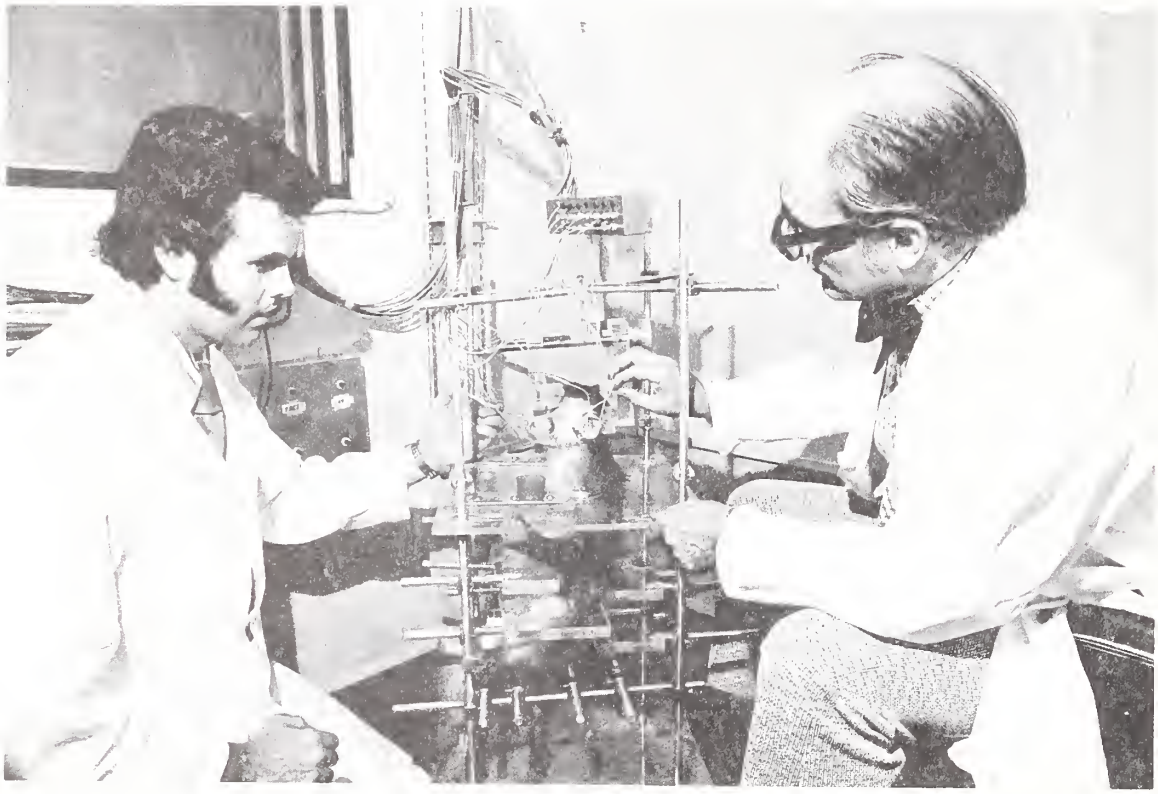
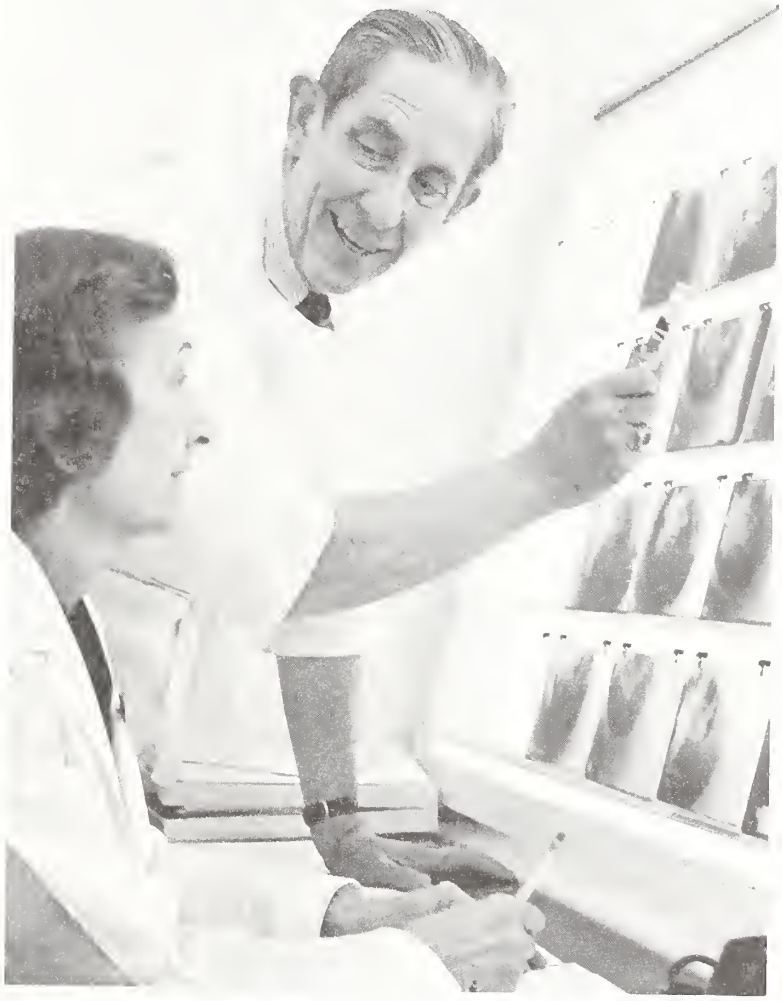
ANN ARBOR, MI--James K. Avery, D.D.S., Ph.D., of the University of Michigan examines slides of micro-sections of palatal tissue. His detailed analyses of palatal shelves at various stages of closure are supported by grants from the National Institute of Dental Research. (NIH Photo #C-1)

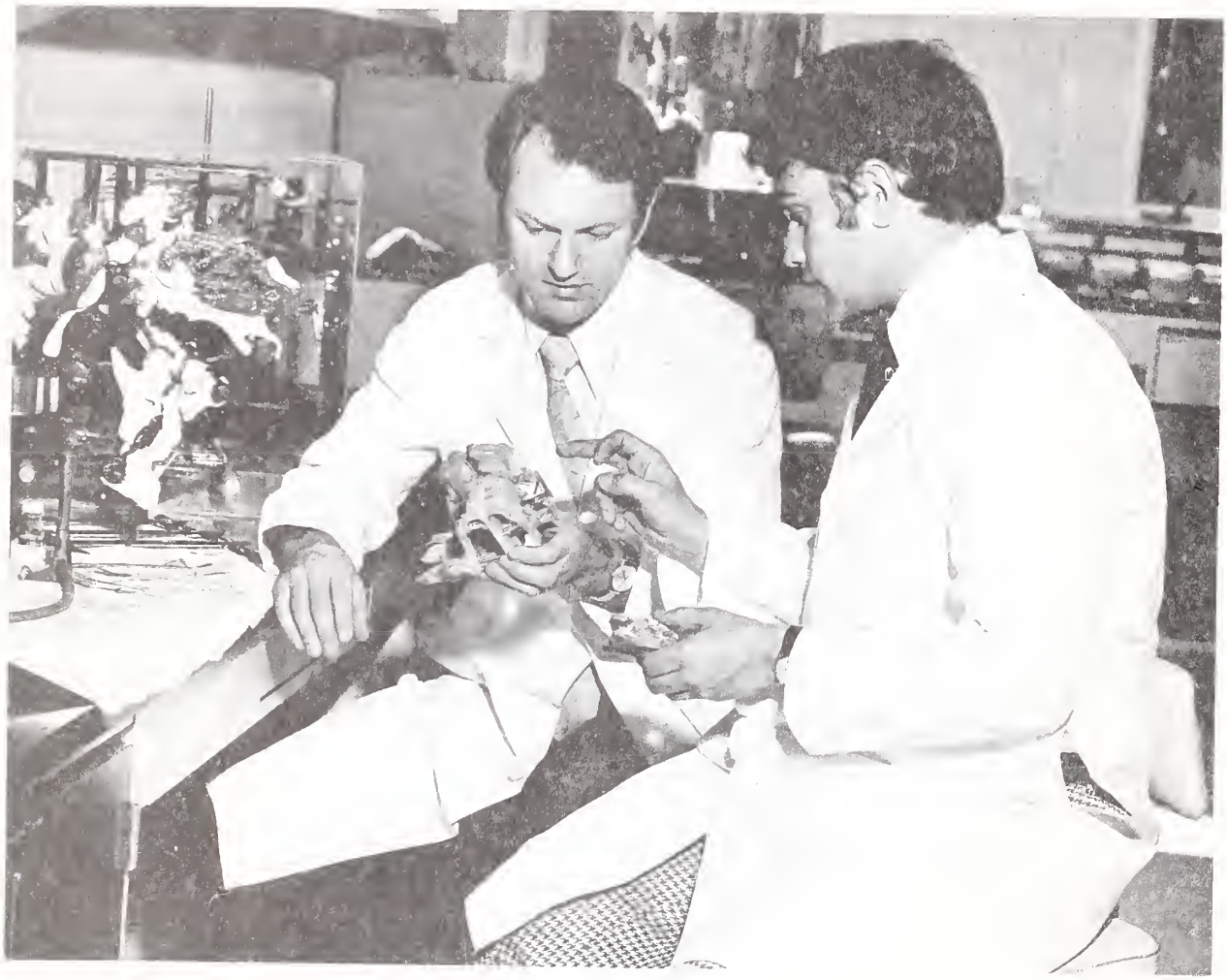


ANN ARBOR, MI--Robert E. Moyers, D.D.S., Ph.D., (right) and James A. McNamara, D.D.S., of the University of Michigan study oral-facial reflexes in swallowing and their relationship to malocclusion. By experimentally producing abnormal function in subhuman primates, the scientists can analyze the compensatory neuromuscular activity and determine whether it causes malocclusion. This research is funded by the National Institute of Dental Research in its efforts to better treat and ultimately to prevent malocclusion. (NIH Photo #C-2)

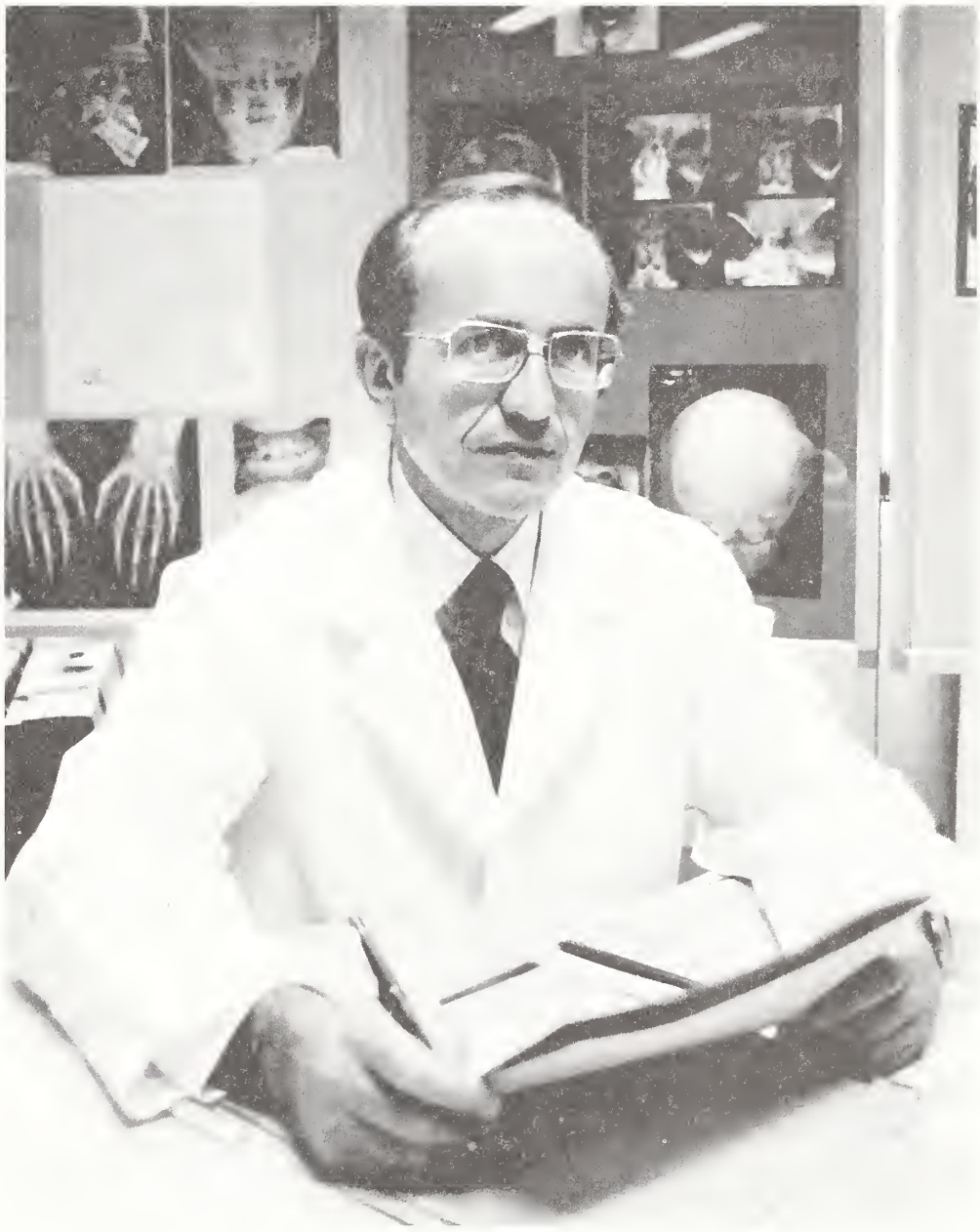
BOSTON



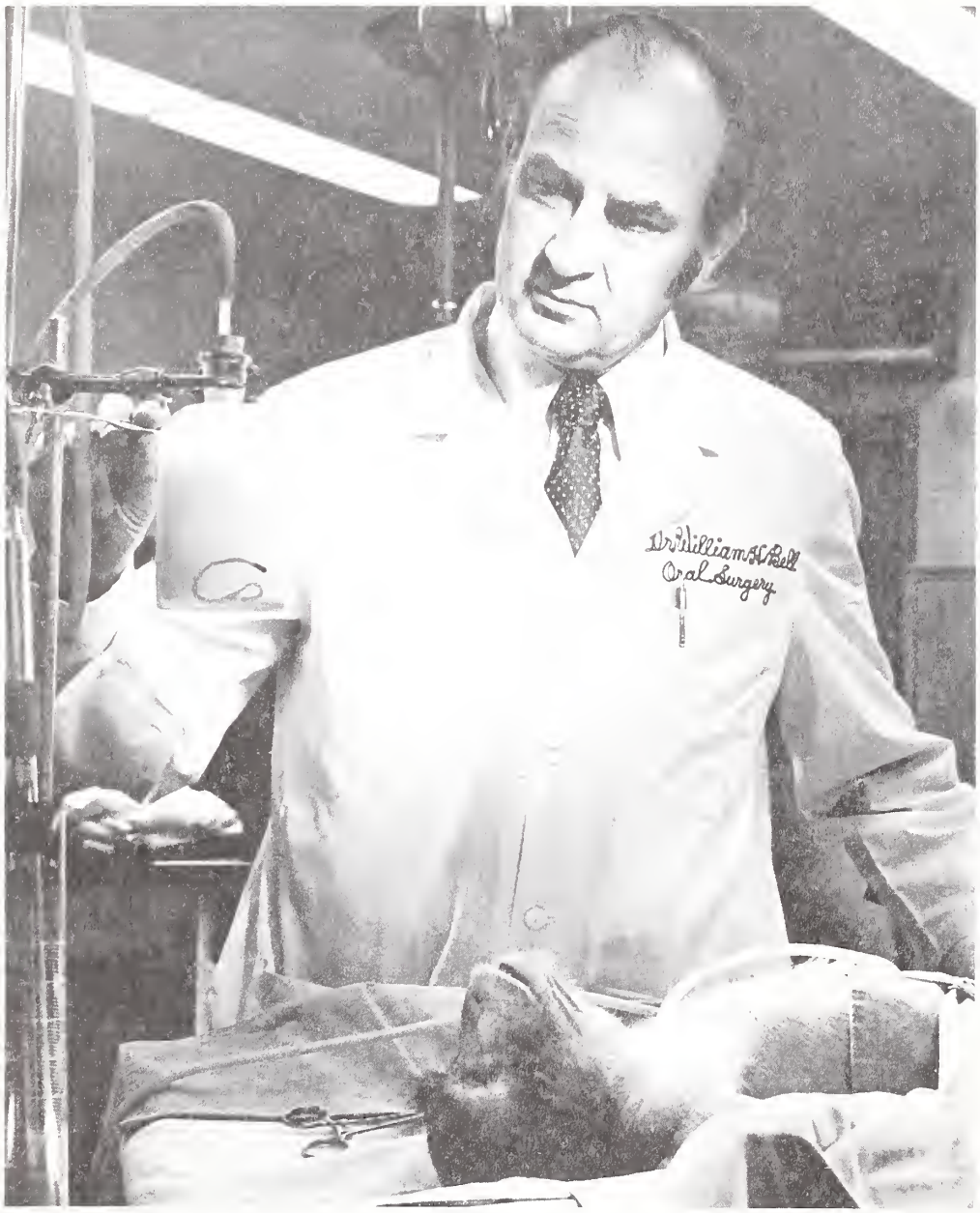
BOSTON, MA--Coenraad F.A. Moorrees, D.D.S., of Harvard University and the Forsyth Dental Center discusses some details of his analyses of facial growth in identical twins. The study, being performed with funds from the National Institute of Dental Research, will help determine the genetic components of cranio-facial form. (NIH Photo #C-3)



CHAPEL HILL, NC--Ralph A. Latham, Ph.D., of the University of North Carolina (left) discusses with Bruce King, a Pfeiffer Research Fellow, the normal anatomy at birth of the cartilages and other tissues of the nose with reference to tissue abnormalities found in people with bilateral cleft lip and palate. Studies using the model held by Dr. Latham are being made with support from the National Institute of Dental Research to better understand growth and development in children with the birth defect. The first step in the understanding of any disease must be an accurate and full clinical description. (NIH Photo #C-4)

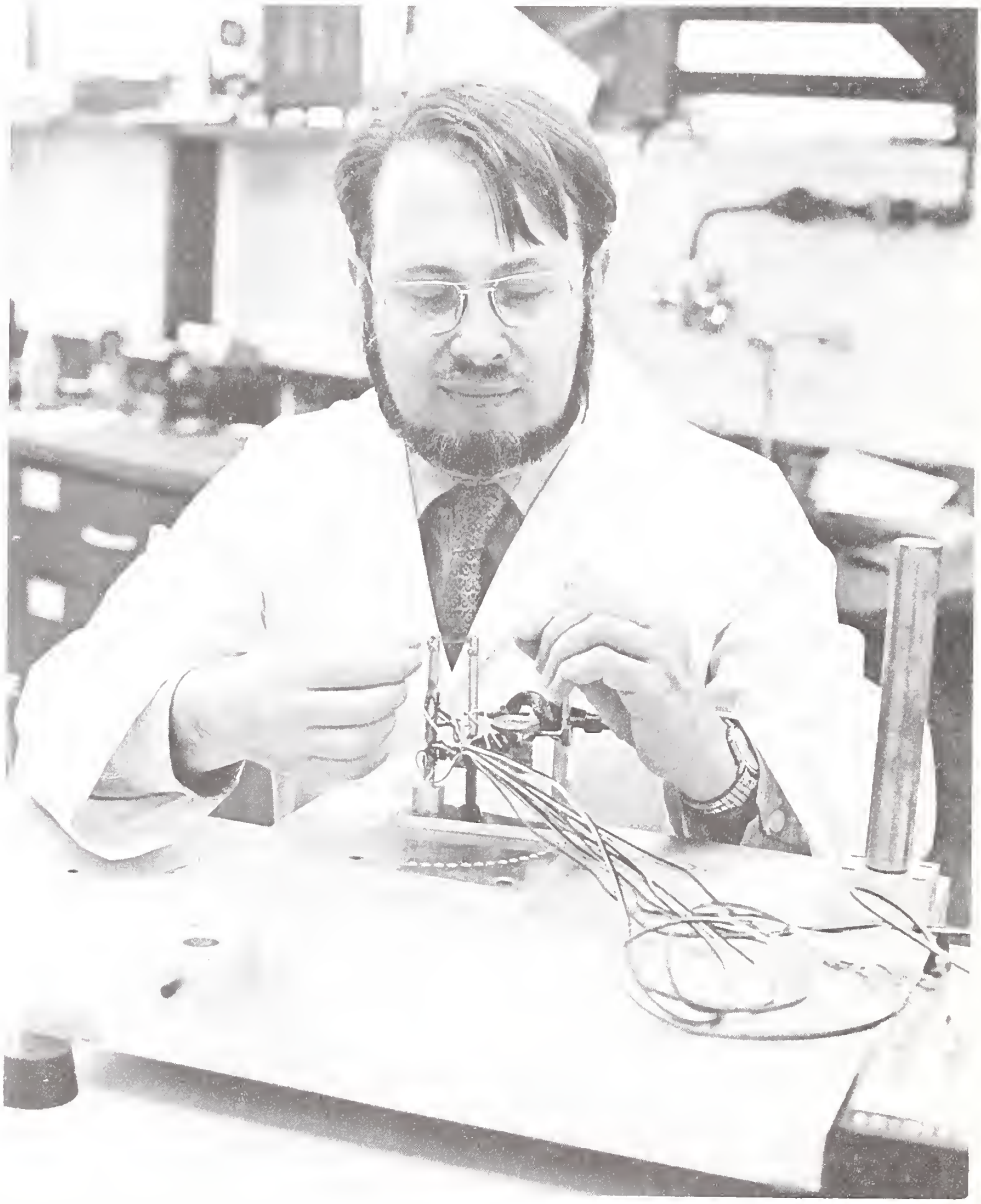


CHICAGO, IL--Long-term growth studies by Samuel Pruzansky, D.D.S., of patients with craniofacial syndromes are essential in defining the primary defects--such as premature fusion of bony sutures--around which complex malformations develop. The findings of research at the University of Illinois Medical Center will lead to improved diagnosis and habilitative procedures. The investigations are funded by the National Institute of Dental Research. (NIH Photo #C-5)

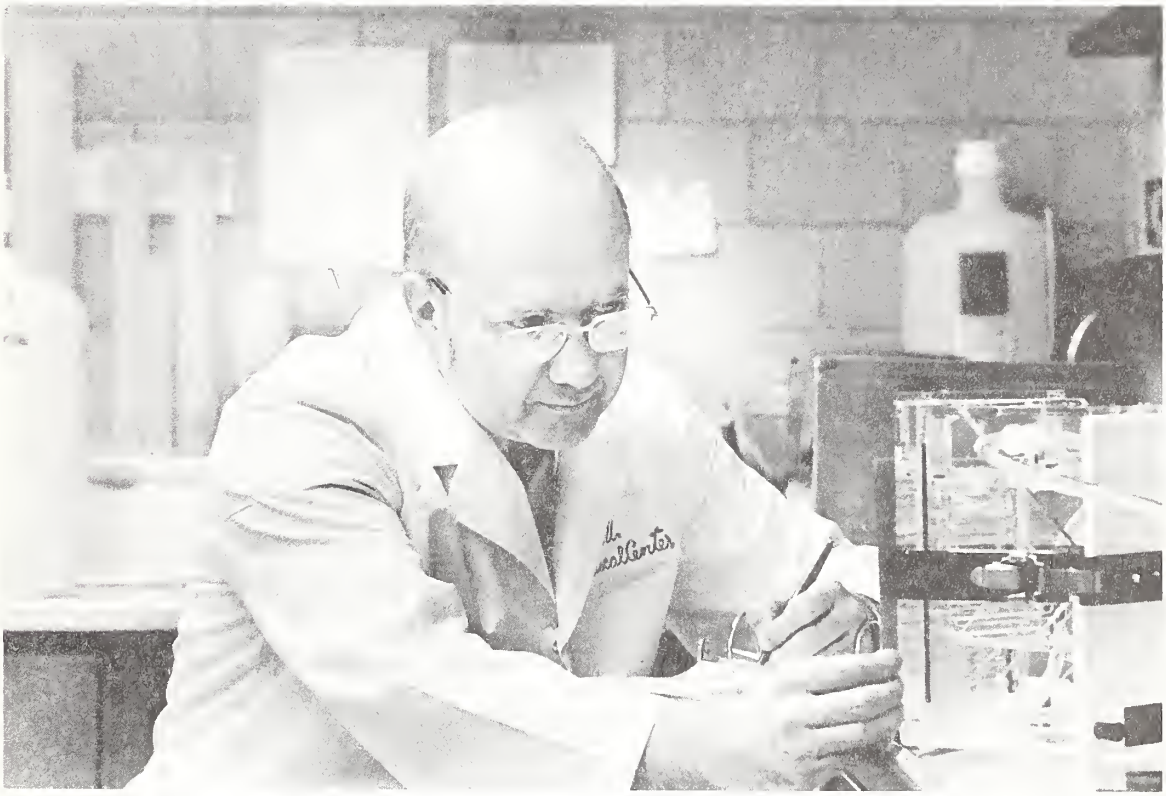


DALLAS, TX--William H. Bell, D.D.S., of the University of Texas Health Science Center performs surgery on facial bones of monkeys and studies the healing process to find ways of preserving the vascular and nerve supply. Studies to improve surgical treatment of craniofacial malformations are supported by the National Institute of Dental Research. (NIH Photo #C-6)

DURHAM, NC--Kenneth L. Pickrell, M.D., is studying craniofacial anomalies in NIH-funded research at the Duke University Medical Center. Dr. Pickrell is chairman and professor, Department of Surgery, Division of Plastic, Maxillofacial, and Oral Surgery. (NIH Photo #C-7)



FARMINGTON, CT--Charles J. Burstone, D.D.S., of the University of Connecticut Health Center is analyzing the force system in a new orthodontic appliance. The National Institute of Dental Research supports his studies of the stress levels within the periodontium created by such appliances. (NIH Photo #C-8)

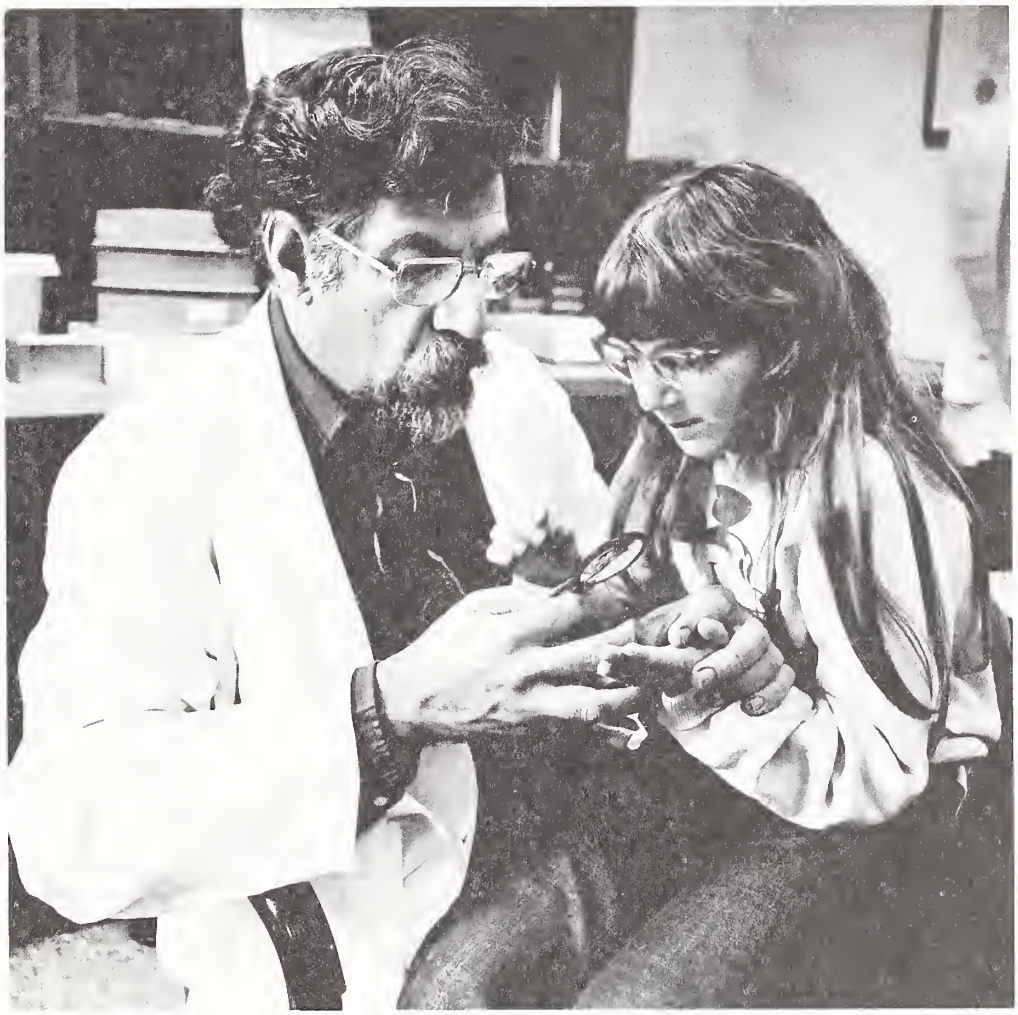


INDIANAPOLIS, IN--David Bixler, D.D.S., Ph.D., of Indiana University is supported by grants from the National Institute of Dental Research in his attempts to elucidate the inheritance patterns of cranio-facial anomalies. Here he is separating serum proteins in an electrical field. Once hereditary patterns of these proteins are established, they can serve as markers for genetic studies. (NIH Photo #C-9)

IOWA CITY, IA--To develop criteria for selection of treatment best suited to the individual patient with a cleft lip or palate, Hughlett L. Morris, Ph.D., (right) and Charles R. Kremenak, Ph.D., (left) of the University of Iowa are integrating data from studies of maxillofacial growth and speech proficiency. The investigators are supported by the National Institute of Dental Research. (NIH Photo #C-10)

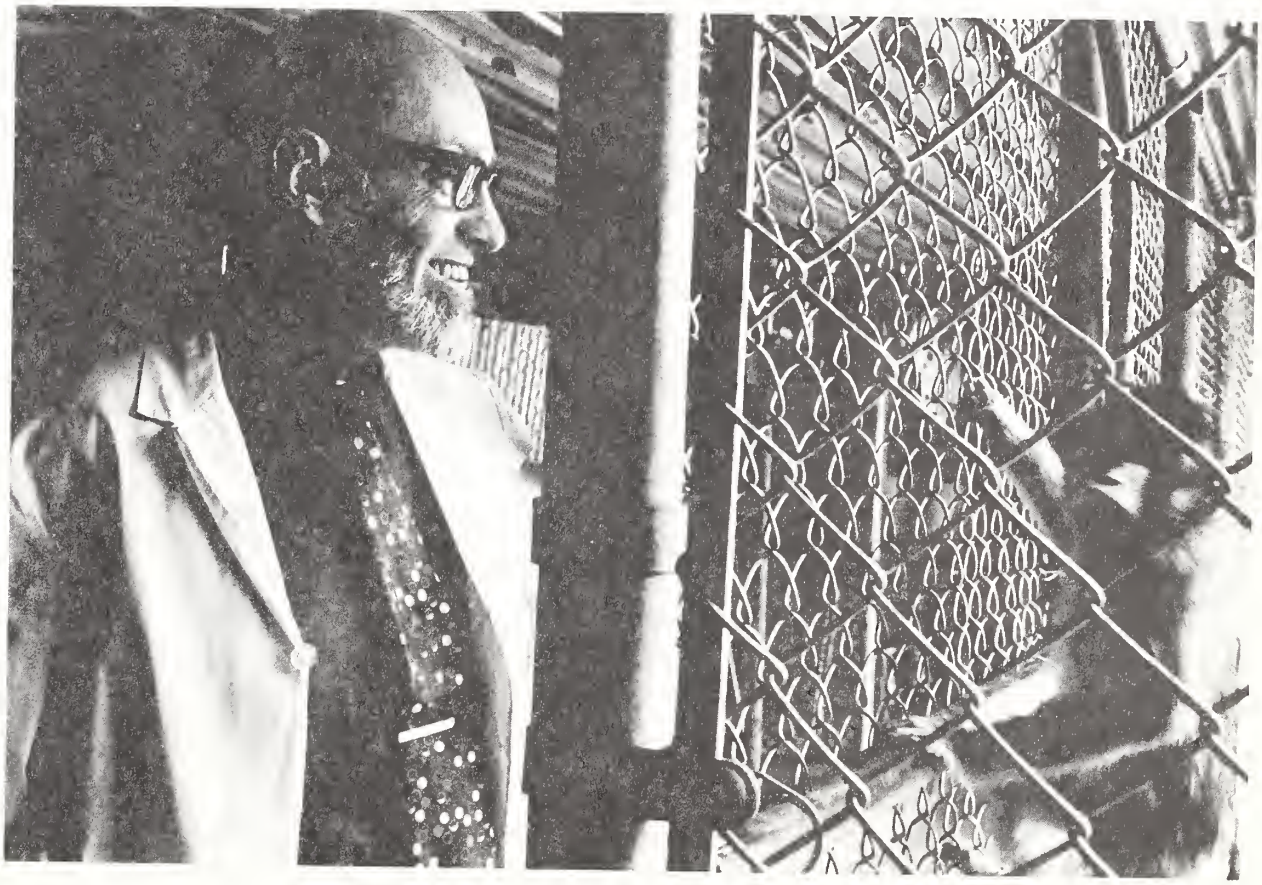
LANCASTER, PA--A research-treatment team at the Lancaster Cleft Palate Clinic compare serial head and dental X-ray films, photos, and dental casts in their research efforts to improve treatment for children born with cleft lip and palate. Their studies are funded by the National Institute of Dental Research. Seated (left to right) W.M. Krogman, D.D.S., H.K. Cooper, Sr., D.D.S., D.Sc., and Mohammad Mazaheri, D.D.S. Standing (left to right) Dennis R. Ranalli, D.D.S., Robert L. Harding, D.D.S., and Robert T. Millard. Left rear is Kathy Zimmerman. (NIH Photo #C-11)

LOS ANGELES, CA--University of Southern California research into the cellular control of craniofacial development is supported by the National Institute of Dental Research. Harold Slavkin, D.D.S., (standing) and Pablo Bringas discuss their team's findings which are clarifying how mesenchyme and epithelial tissues interact during differentiation in the embryo. (NIH Photo #C-12)

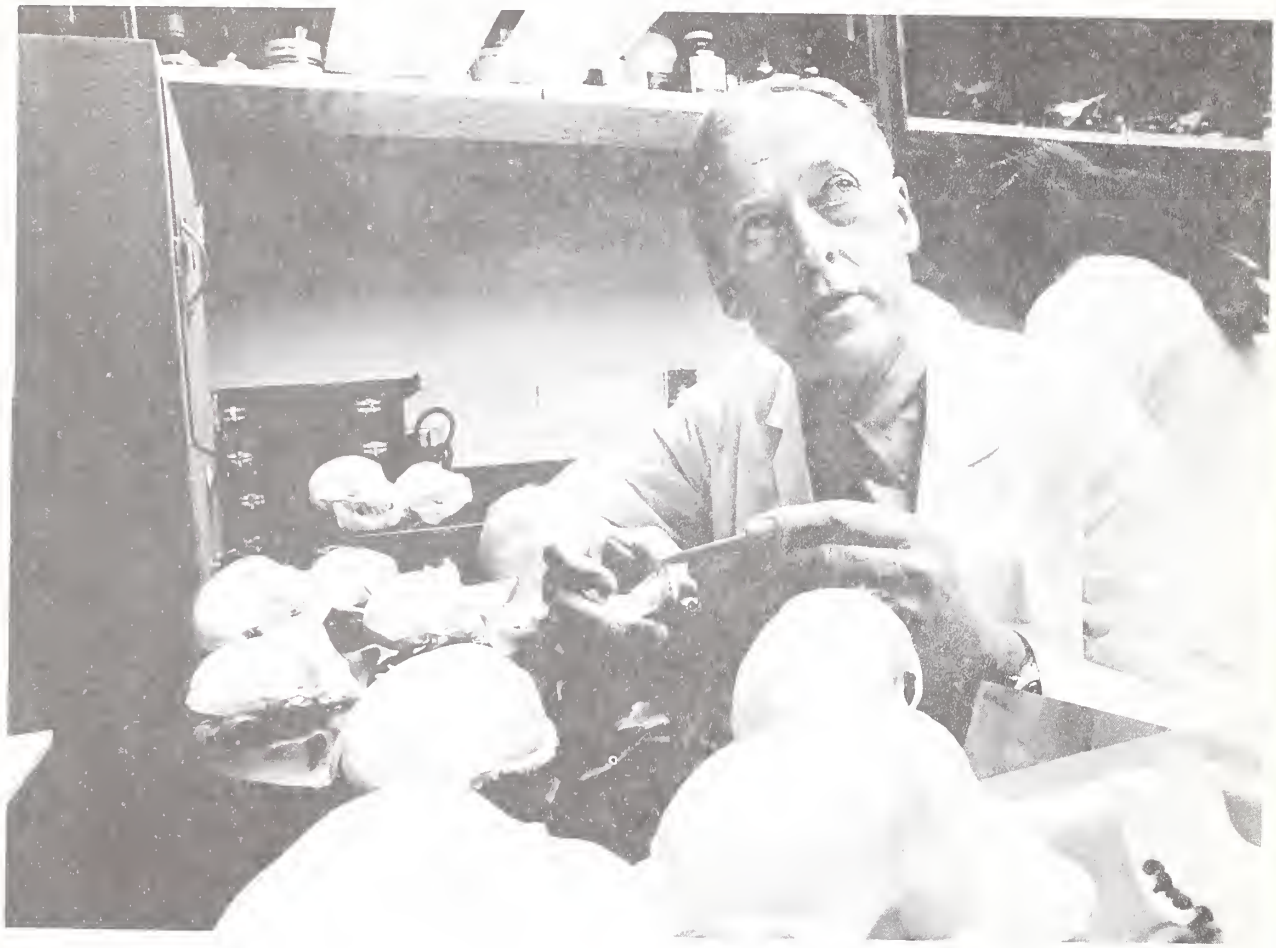


MINNEAPOLIS, MN--Studies by Robert J. Gorlin, D.D.S., of the University of Minnesota are showing that syndromes which appear to be confined to craniofacial abnormalities also involve other defects as well. Dr. Gorlin has found abnormalities in palm prints of children with a variety of craniofacial syndromes. This project and a variety of others are supported by the National Institute of Dental Research to understand the cause of such birth defects. (NIH Photo #C-13)

SAN FRANCISCO, CA--Egil P. Harvold, D.D.S., Ph.D., of the University of California has applied some principles gained from his experiments with craniofacial orthopedics in monkeys to innovative treatment of children with deformed mandibles (lower jaws). His research is supported by the National Institute of Dental Research. (NIH Photo #C-14)



SEATTLE, WA--Dr. Benjamin C. Moffett, Jr., Ph.D., visits a colony of Macaca Nemenstrini *on the roof of the Northwest Regional Primate Center at the University of Washington. Groups of these monkeys are used by Dr. Moffett and other investigators to study oral-facial growth and development under a grant from the National Institute of Dental Research. Periodic radiographic analysis creates a pictorial sequence of cranial-facial development. Other monkeys are used to study the influence of applied forces on development and the effect of selective tooth extraction in early years upon orthodontic problems. (NIH Photo #C-15)*

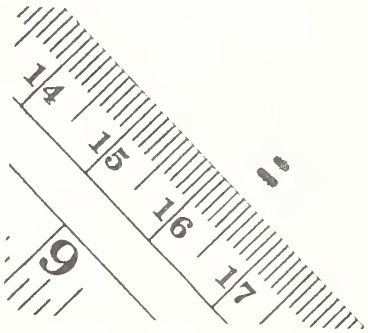


SEATTLE, WA--Alton W. Moore, D.D.S., points to a monkey condyle--the part of the lower jaw that joins the skull forming the temporomandibular joint. Alteration of this joint is important in experimental orthodontic procedures aimed at controlling the form of the lower jaw to improve occlusion between upper and lower teeth. These skulls represent normal development at various stages and are being studied under a grant from the National Institute of Dental Research to the scientist at the University of Washington. Such detailed studies are possible because the monkeys are born and bred at the University permitting exact knowledge of genetics, age, and rearing circumstances and assuring freedom from disease. (NIH Photo #C-16)

NEWS&FEATURES FROM NIH

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE ■ Public Health Service ■ National Institutes of Health ■ Office of Information ■ Bethesda, Maryland 20014

September 25, 1973



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NEWS & FEATURES From NIH September 25, 1973

Research Advances

SYNTHETIC ANTIGEN MODIFIES TUMOR GROWTH IN ANIMALS

Using highly sophisticated laboratory techniques, an NIH-supported scientist at the Salk Institute in California has manufactured a chemical substance--an antigen--which mimics antigens found on the surface of some tumor cells. According to W.T. Shier, Ph.D., use of the synthetic antigen as an immunizing agent protected rats against a transplanted tumor and was of some benefit to mice with a different kind of cancer.

Many disease-causing agents escape detection by the body's immune system because the chemical structures (antigens) on their surfaces are not "foreign" enough to elicit an adequate immune response. Scientists have theorized that if a weak antigen can be attached to a carrier which the body *can* recognize, a protective immune response will be elicited when the animal is exposed to the carrier-antigen complex. This has been called the "chemical vaccine" approach and it is believed to offer some hope for the control of some cancers.

Dr. Shier reports that he first determined that the antigen found on some tumor cells belongs to a class of chemicals known as glycoproteins. From the blood of an Antarctic fish, he extracted appropriate glycoproteins and converted them into a form suitable for testing as a synthetic tumor-specific antigen. This synthetic antigen, called FA, was then treated with methylated bovine serum albumin (MBSA) and the complex FA(MBSA) was formed.

The effectiveness of the carrier-antigen complex as an immunizing agent, or vaccine, was evaluated in a series of experiments in which rats were given solutions of varying amounts of FA(MBSA) or MBSA alone. Each animal received

(more)

an initial injection, then a booster two weeks later. Three weeks after the booster injection, cells of a chemically-induced rat breast tumor were transplanted in the animals.

Protection against the transplanted tumor was observed with the lowest levels of FA(MBSA) given, while enhancement of tumor growth was found with higher levels of the immunizing complex. These results, obtained with the synthetic antigen, are consistent with those observed when tumor-specific antigens themselves have been used as immunizing agents.

Dr. Shier, whose work is supported by a National Institute of Allergy and Infectious Diseases grant and a National Cancer Institute contract, explains that lower levels of a glycoprotein antigen favor the production of a cell-mediated immune response--that part of the total response which is mediated by small lymphocytes (white cells) and is responsible for reactions such as graft rejection. Higher levels of a glycoprotein antigen favor the production of a humoral response--specific immunity which is mediated by blood proteins known as antibodies. It is not yet known why tumor enhancement, under these circumstances, takes place.

Experiments similar to the above were also carried out in mice challenged with myeloma cells. Although only minimal protection by FA(MBSA) was observed, further study revealed that protection was specific, that is, directed only against tumor cells and not against normal cells. This observation lends support to the suggestion that tumor cells do differ from normal cells in the number or distribution of glycoprotein antigens found on their surfaces--an important difference which may, eventually, be exploited in the treatment or

(more)

Antigen (Cont'd)

prevention of human tumors.

Dr. Shier published a report of his findings in the July 13, 1973 issue of *Nature*.

#

Research Advances

NEW EVIDENCE CONTRADICTS CONNECTIVE TISSUE THEORY

Scientists have provided valuable new insight into the function of hydroxyproline, an amino acid occurring primarily in collagen, the body's most abundant protein and essential ingredient in holding together bones, skin, teeth, and blood vessels.

Headed by Joel Rosenbloom, M.D., Ph.D., associate professor of biochemistry at the University of Pennsylvania School of Dental Medicine, a research team has produced evidence contradicting the prevalent belief that hydroxyproline is inessential to the structure integrity of the collagen molecule.

Through a variety of experiments, the team at the University's Center for Oral Health Research (COHR) has shown that hydroxyproline-deficient molecules do not form triple-helices (the normal state of the collagen molecule, in which three poly-peptide chains wind around each other forming a rope-like structure) at normal body temperatures and appear instead as denatured chains.

The denatured molecules are secreted at a slower rate than are hydroxylated triple helical molecules and cannot form normal collagen fibrils, thereby destroying collagen's important connective properties.

While additional research is planned, Dr. Rosenbloom and colleagues report that their findings relate to a number of research areas.

For example, the findings may help explain what happens biochemically in scurvy, as ascorbate (Vitamin C) deficiency disease in which collagen formation

(more)

Connective Tissue (Cont'd)

is impaired and tissues break down. Vitamin C is also necessary for hydroxyproline production, and its deficiency may impede collagen secretion by first limiting hydroxylation.

Also, the study findings may be useful in the investigation of a number of genetic diseases (such as Ehlers-Danlos syndrome) which are related to the breakdown or dysfunction of connective tissue.

Dr. Rosenbloom reports that his studies of hydroxyproline may also be useful for comparative biochemical studies of collagen, indicating, for example, that the temperature of an organism may partially regulate the degree of hydroxylation of collagen. Therefore, organisms with lower body temperatures may naturally have a lower degree of hydroxylation.

The investigators also speculate that the findings may relate to the study of a variety of diseases stemming from the same conditions which can create underhydroxylation in proline (ascorbic acid, oxygen, or iron deficiency).

Collagen, which forms the framework of connective tissue and the substructure of bone tissue and detine in teeth, is synthesized intracellularly and is then secreted into intercellular spaces. In another intracellular process, hydroxyproline is produced from the imino acid, proline, after the proline has been incorporated into peptide linkage. The hydroxylation can be inhibited by limiting any of three enzymatic co-factors--oxygen, iron, or ascorbic acid.

In previous experiments, Dr. Rosenbloom and Darwin J. Prochop, M.D., Ph.D., (formerly with the National Heart and Lung Institute and now at Rutgers

(more)

University) found that underhydroxylated molecules of collagen were secreted at a markedly reduced rate. According to Dr. Rosenbloom, "These experiments suggested that hydroxyproline was performing some role in the secretion of collagen." The precise role is still uncertain, however. Later experiments by Beverly Peterkofsky, Ph.D., of the National Cancer Institute, produced similar results in collagen secretion when ascorbic acid was limited.

In response to such findings, the COHR team began a number of experiments. Earlier work showing that formation of the triple-helix occurs intracellularly before collagen is secreted suggested a possible connection between formation of the triple-helix and hydroxyproline formation.

Using collagen isolated from fibroblasts in chick tendon, Dr. Rosenbloom tested the thermal stability of unhydroxylated collagen relative to hydroxylated collagen. Unhydroxylated collagen thermally denatured at 20 to 25 degrees centigrade (C), while hydroxylated was stable to at least 35 degrees C, suggesting that hydroxyproline might be necessary for collagen stability at normal body temperatures (37 degrees C) and that the triple strand formation might be needed for normal secretion.

Next, the COHR team performed a series of thermal stability tests on nine collagen samples whose hydroxyproline content varied from less than one to 100 percent of the normal level. The denaturation temperatures of the collagens proved to be directly proportional to the hydroxyproline content--again suggesting that hydroxyproline contributes significantly to the thermal stability of the triple-helix and that hydroxyproline-deficient molecules may be denatured in cells and tissues at body temperatures.

(more)

Connective Tissue (Cont'd)

Finally, working with the mouse fibroblast, the team found that this is precisely what occurs. In three different experimental conditions, they showed that hydroxyproline-deficient collagen molecules do not form triple-helices at 37 degrees C and are found in culture as denatured chains.

Dr. Rosenbloom's studies are supported by the National Institute of Dental Research. He published an initial report of his findings in the May 1973 issue of *Biochemical & Biophysical Research Communications*.

#

Research Advances

Research In Progress...

TRANSPLANT OF BRAIN CELLS SUCCEEDS IN YOUNG ANIMALS

Embryonic brain cells have for the first time been successfully transplanted in young animals in a National Institute of Neurological Diseases and Stroke-supported research program at Purdue University.

The transplanted immature brain cells became functional and were not rejected by the host cells. These results demonstrate that transplantation of nerve cells is possible as long as the donor cells are immature or undifferentiated, and the host brains are still developing.

While this work is still at the basic research stage, the scientists stress that the results are a highly encouraging step in understanding and correcting brain injury.

The team also demonstrated that during the embryonic development of the brain, different nerve cells evolve at specified times and from specified regions of the brain. Investigators believe this embryonic data may be vitally important in aiding clinicians to better understand and correct damage or abnormalities in the developing brain.

Another important finding was that the young brain displays considerable powers of functional regeneration of damaged areas through rearrangement of nerve cells. This was demonstrated by the fact that damage to developing brain cells did not necessarily destroy the function of that part of the brain.

(more)

Transplant (Cont'd)

The Purdue scientists, under Gopal D. Das, Ph.D., of the Department of Biological Sciences, "tracked" the neurons through use of a radioactive chemical called tritiated thymidine. Since nerve cells formed in the embryonic period never multiply, labeling the neurons with a radioactive tag allows them to be traced throughout their life span.

The scientists observed that most types of immature nerve cells can be successfully transplanted into any developing region of the brain. However, the transplanted cells retain their unique properties rather than adopt those of the host.

Since the brain, unlike other tissues of the body, lacks the capacity to physically repair itself, transplantation could be a viable alternative. To date, transplantation of the brain in mammals has been regarded as an impossibility. Significantly, this work has shown that at a cellular level, transplantation is possible.

#

NEWS & FEATURES From NIH September 25, 1973

Photo Feature

NIH SCIENTISTS HELP DEVELOP MASS SPECTRAL SEARCH SYSTEM

A computer technique, developed by National Institutes of Health scientists to evaluate drug overdoses, has led to the establishment of a readily-available world-wide data bank.

Any scientist with a teletype machine and an acoustic coupler can use the new, conversational mass spectral search system. The system was developed by Stephen R. Heller, Ph.D., of the NIH Division of Computer Research and Technology, and by Henry M. Fales, Ph.D., and George W.A. Milne, Ph.D., of the National Heart and Lung Institute.

In the system, a gas chromatograph rapidly separates compounds from one another and also from normal components of biological fluids. As the pure compounds emerge--one by one--from the column of the gas chromatograph, they enter the second part of the instrument: a mass spectrometer. Here the compounds are bombarded by electrons to produce a complex signal--called a mass spectrum--which provides a very precise "fingerprint" of the compound in question.

The mass spectrum of an unknown compound is read by a computer that searches through its master file to match the spectrum, and therefore identify the "fingerprint."

The system options include a peak/intensity search, molecular weight search, complete and imbedded molecular formula searches, and printout, display, microfiche, or plotting of the peaks and intensities of the entire spectrum.

(more)

Search System (Cont'd)

The computer search procedure was developed by NIH scientists and uses a data base compiled by the Mass Spectrometry Data Centre (MSDC), Aldermaston, England. The enthusiastic interest generated by more than 200 scientists around the country from this interagency cooperative experiment has led to the MSDC taking responsibility for the system, while NIH scientists continue their research and development efforts on other related computer applications. The MSDC has chosen the General Electric international computer network on which to run the system.

In earlier NIH research, Drs. Fales and Milne developed a technique that, usually within an hour, can determine which drugs and how much a patient has ingested.

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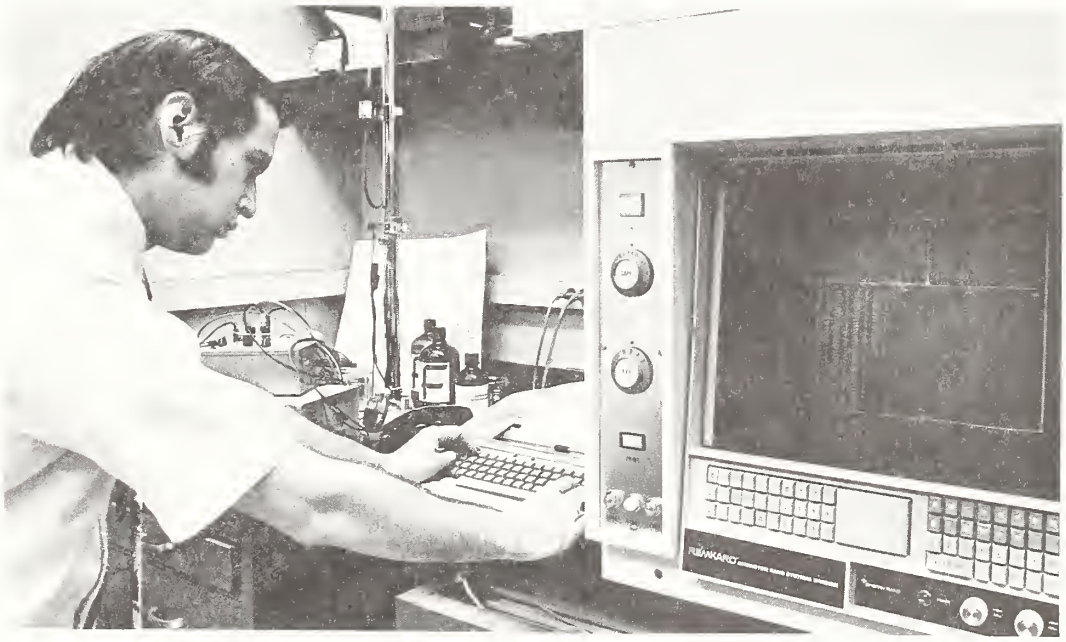

Stephen R. Heller, Ph.D., of the NIH Division of Computer Research and Technology, is shown at the computer terminal of a new, conversational mass spectral search system. He and other NIH scientists helped develop the system. A mass spectrum is shown on the screen at right. (NIH Photo #1130)

Search System (Cont'd)

The system can also help determine if a drug is in the patient's stomach or in the bloodstream. This fact, combined with the specifics of the drugs taken, helps physicians at local hospitals determine the treatment to be followed.

#

News Feature

CORONAVIRUSES MAY CAUSE MANY ADULT WINTER COLDS

One sure sign of winter's approach, and an unwelcome occurrence other times of the year as well, is the common cold. Though a mild illness, it is one which has so far defied all efforts at control or cure.

Headache, sneezing, stuffy nose, sore throat, a general feeling of fatigue, coughing, and sniffles are the symptoms of the common cold. It is uncommon for temperatures to increase more than one degree in adults or to go higher than 102° in children. The common cold normally runs its course, with only symptomatic treatment such as aspirin and rest, in two to seven days. If colds occur frequently, or last much longer than a week, they may not be colds at all, but allergies of sinus infections. Coughs, particularly if prolonged, may also indicate more serious infection.

The National Center for Health Statistics reports that more than 90 million colds occurred in a one-year period beginning July, 1967 in the United States, accounting for 25 percent of all acute illnesses. These colds resulted in some 234 million days of restricted activity, a loss of 36 million school days and 32 million work days. Other estimates of the annual incidence indicate an average of eight colds per year for children under four years of age and two colds per year for adults for a total of as many as one billion colds per year. In any case, statistics do not adequately reflect the toll in reduced vitality, decreased efficiency, and below-standard productivity. The dollar cost of respiratory pharmaceuticals--pills and formulas for relief of runny noses or stuffed-up heads--is estimated at more than $550 million per year.

(more)

Colds (Cont'd)

Almost all colds are believed to be caused by viruses, but only one-third to one-half of the colds which occur can be blamed on a specific virus. In the other colds studied, no agent has been isolated. Recently, scientists using different laboratory methods of growing infectious agents have succeeded in isolating viruses from patients with colds for which no agent had been previously discovered.

The rhinoviruses were the first important group of viruses to be associated with the common cold in adults. These agents cause one-fourth to one-third of all colds. Now, a new group, the coronaviruses, has emerged as a possible important cause of adult colds occurring from December through February--a period when rhinoviruses are uncommon.

Other viruses which can cause "common cold" symptoms but are associated with more serious illnesses as well are the myxoviruses (which include the influenza and other viruses as well), the paramyxoviruses, the adenoviruses, and the enteroviruses. The enteroviruses are composed of the polio, coxsackie, and echoviruses.

Direct contact with a person who has a cold is the best way to "catch" the disease. Rhinoviruses are transmitted by close contact via nasal and throat secretions of the infected person, primarily through sneezes or coughs which spray the viruses into the air where they hang, ready to be inhaled by someone in the same car, at the same table, or at the next desk.

Because rhinoviruses are the chief known causes, they are the focus of a three-pronged attack on the common cold by the National Institute of Allergy and Infectious Diseases (NIAID) through its intramural research laboratories,

(more)

its collaborative contract programs, and its support of grantee investigators across the country.

Through cooperative efforts of NIAID scientists and other virologists, 89 distinct rhinovirus types have already been classified. Efforts are directed toward isolating them, learning their roles in disease, and determining whether any of the rhinoviruses may be responsible for more colds than others. Results of this latter effort have been disappointing as numerous serotypes appear to be associated with outbreaks of upper respiratory infections. The coordination of a vast collaborative program, aimed at defining the number of rhinovirus serotypes, has been the responsibility of NIAID's Laboratory of Infectious Diseases, which is designated by the World Health Organization as an International Reference Center for Respiratory Diseases Other Than Influenza.

Scientists have recently found several viruses different from rhinoviruses that seemed also to be associated with the common cold. These have now been shown to belong to a common group, the coronaviruses, the first of which was recovered by scientists in England. Thus far, 24 coronavirus strains have been described.

In studies conducted with volunteers in England, scientists have found that the incubation period of a coronavirus cold is usually about one day longer and the period of illness slightly shorter than that of the average rhinovirus cold. Nasal discharge or congestion is the chief complaint in a coronavirus cold, while nasal discharge and sneezing are the primary problems of a cold caused by a rhinovirus.

(more)

Colds (Cont'd)

One difficulty encountered in isolating and identifying a coronavirus is the problem of growing these viruses. Certain coronavirus strains seem to prefer organ cultures to tissue culture cell monolayers, the technique usually used for growing viruses. Organ cultures consist of small amounts of human fetal trachea or nasal mucosa in which the virus is grown in petri dishes in the laboratory. This technique was first used in England and later at the NIAID laboratories to grow certain of the viruses that were subsequently grouped under the term coronavirus.

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Photo Feature

Update...

SICK INFANTS AIRLIFTED TO PREMATURE RESEARCH CENTER

Some West Coast newborns take their first flight on the day they are born--but it is strictly not for pleasure. Most of the infants have breathing problems or require major surgery.

In the last two years, about 120 babies have been transferred by air to the intensive care nurseries at Stanford University Medical Center. Most of the airborne emergency patients have been brought by helicopter to a heliport that is 700 feet from the emergency room entrance. Others were brought longer distances by fixed-wing aircraft, then transported by ambulance.

The helicopter service is part of an interhospital transport system for rapid transfer of critically-ill newborns designed and managed by Philip Sunshine, M.D., Alvin Hackel, M.D., and John Johnson, M.D., of the Departments of Pediatrics and Anesthesia.

The infants selected for placement in the Premature Research Center receive care that is supported by the Division of Research Resources of the National Institutes of Health.

"The transfer between hospitals should be as quick as possible since complete intensive care is not possible until the baby is at Stanford. The ideal traveling time between hospitals is less than one hour," said Dr. Sunshine who is the Center's program director.

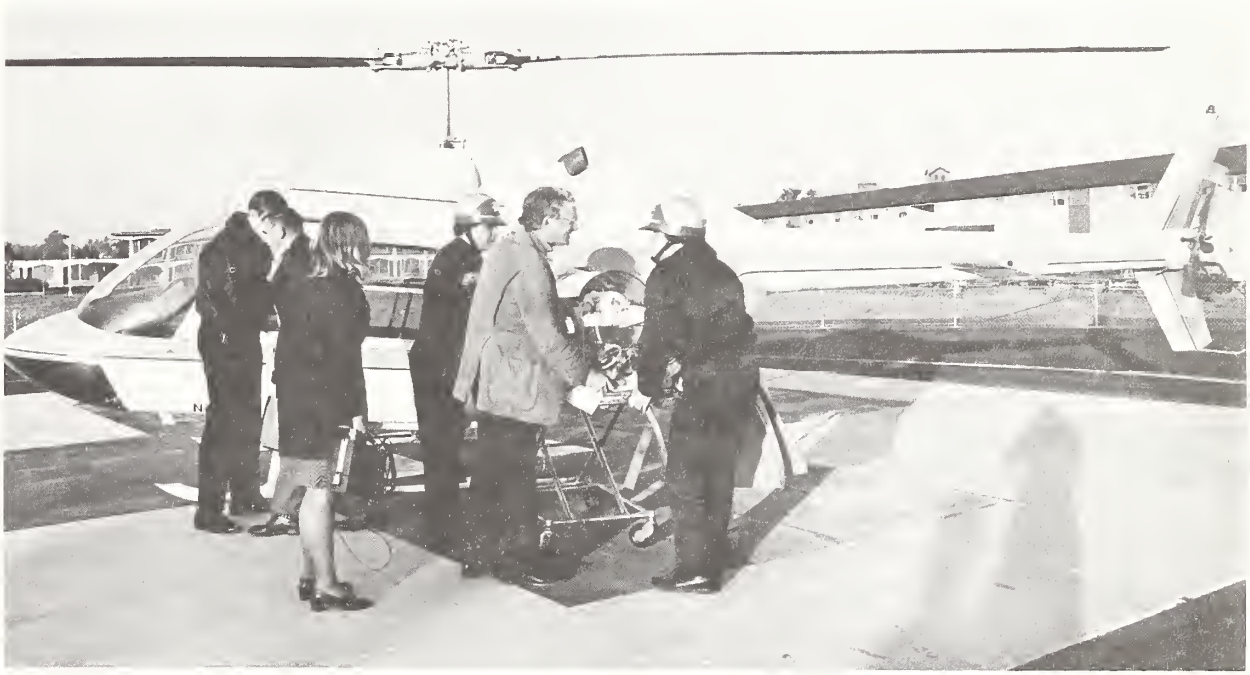
For air transport, special lightweight equipment had to be designed. The Premature Research Center worked with the Department of Anesthesia and

(more)

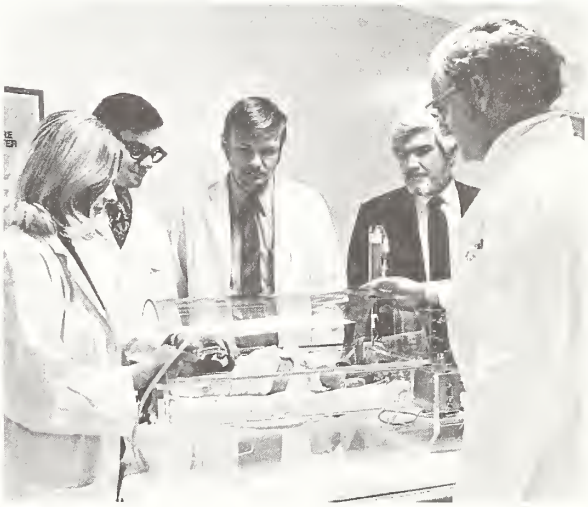
Airlift (Cont'd)

the Thermosciences Division of the University's Department of Mechanical Engineering to modify and adapt the basic neonatal transport unit for use in helicopters and airplanes.

Since infants have not yet developed the ability to ward off cold and maintain a stable body temperature, they must be transported in a neutral



A helicopter (above) brings an acutely-ill newborn to the NIH-funded Premature Research Center at Stanford University Medical Center. Alvin Hackel, M.D. (second from right), headed the transport team on this trip. In the Center (right photo), an infant receives oxygen from Nancy Edwards, M.D. Also shown are (from left) Arnold Goldstein, M.D., John Johnson, M.D., Robert Moffat, M.D., and Alvin Hackel, M.D. The NIH Division of Research Resources provides funds for the Center. (NIH Photos #1131, 1132)



(more)

Airlift (Cont'd)

thermal environment. The Stanford infant transporter provides a comfortable temperature for the infant through the use of radiant heat warmers, a principle adapted from the Apollo space program.

The transporter has an oxygen ventilation system that will supply two to three hours of oxygen, battery powered monitors for heart rate, fluid intake, blood pressure, and temperature; portable rechargeable battery units for the systems; and a stabilizing unit to prevent injury to the infant during sudden changes in speed or altitude. These features are still being streamlined and improved, according to Dr. Sunshine.

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NEWS & FEATURES From NIH September 25, 1973

Medical News Tip

NODULES CHARACTERISTIC OF SARCOIDOSIS--Although Sarcoidosis (Boeck's sarcoid) was recognized nearly a century ago, its cause has not yet been determined.

Sarcoidosis is marked by the appearance, almost anywhere in the body, of characteristic small lumps (nodules). Lungs, lymph nodes, liver, spleen, eyes, and skin are most frequently involved. Nodules may be sparse or numerous. Even when a great many nodules are present, however, the disease is rarely fatal.

Although sarcoidosis is encountered throughout the world, estimates of its prevalence indicate wide variation from country to country. Sweden appears to have the highest rate--64 per 100,000--while nearby Finland has one of the lowest. In the United States, sarcoidosis attacks blacks and residents of rural areas with an especially high frequency. Although it occurs in all age groups, the disease is most often seen in persons between the ages of 20 and 40. Susceptibility does not appear to be inherited, nor is there evidence that the disease is contagious.

For additional information, contact:

National Institute of Allergy and Infectious Diseases Information Office
Building 31, Room 7A-32
NIH, Bethesda, MD 20014
Phone (301) 496-5717

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Capsules

Factual Fillers

COLLATERAL CIRCULATION--Nature has her own remarkable way of averting disaster even though the coronary arteries have started to harden--"collateral circulation." Neighboring arteries carry more blood than formerly to compensate for a narrowed vessel, and new arterial branches open up to help transport blood to where it is needed, according to the National Institutes of Health.

ARTERY HARDENING--Every artery throughout the body is subject to hardening, but the most often and most seriously affected vessels are the largest arteries, such as the aorta; the coronary arteries, and the arteries that feed the brain and kidneys. Arteries may harden in one part of the body more rapidly than in other areas, according to the National Institutes of Health.

CARDIOVASCULAR SYSTEM--The body's circulatory system--also called the cardiovascular system--is made up of the heart and the arteries, capillaries, and veins. The heart contracts about 70 times each minute, pumping oxygen- and food-rich blood into all regions of the body to nourish the muscles and tissues, according to the National Institutes of Health.

EARLY START--Hardening of the arteries may actually begin in early youth, perhaps even at birth. How troublesome it eventually becomes varies with each individual who has it. Some escape any consequence of the condition whatsoever. Others develop some symptoms, but with proper medical care

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Factual Fillers (Cont'd)

continue normal and productive lives, according to the National Institutes of Health.

EMPHYSEMA--Life expectancy is reduced by circulatory complications combined with emphysema. Especially serious are such added problems as right-heart "overwork" owing to high blood pressure in the pulmonary blood vessels and an abnormal increase in the number of red blood cells, according to the National Institutes of Health.

RHEUMATIC FEVER--Although the cause of rheumatic fever is not fully known, research has shown that most rheumatic fever cases are preceded by "strep" infections of the throat, nose, or tonsils, according to the National Institutes of Health.

SORE THROAT--Penicillin and certain other antibiotics are effective destroyers of the streptococcus germ. Used promptly according to the doctor's orders whenever a sore throat or tonsillitis strikes, they can usually prevent the first attack of rheumatic fever, according to the National Institutes of Health.

CLOGGED ARTERIES--Hardening of the arteries sets the stage for many strokes by clogging arteries carrying blood to the brain. The damaged artery or arteries may be located either inside the brain or in the neck, according to the National Institutes of Health.

Factual Fillers (Cont'd)

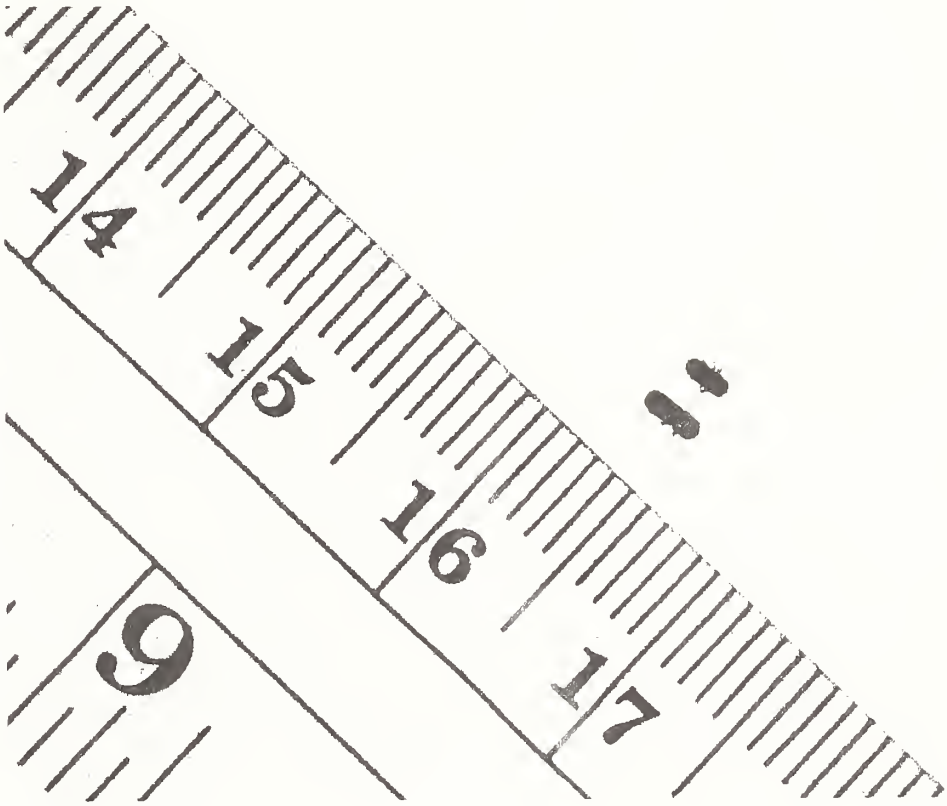
SICKLE CELL--Sickle cell trait, the generally harmless condition, occurs about once in every ten American blacks. Sickle cell anemia occurs about once in every 500 American blacks. At present, it is estimated that there are about 50,000 persons in the United States with sickle cell anemia and about two million with sickle cell trait, according to the National Institutes of Health.

HEMOGLOBIN--The term "sickle cell disease" refers to all inherited blood conditions in which sickle cell hemoglobin is present. Hemoglobin is the red colored substance in red cells that enables blood to carry oxygen from the lungs to all tissues of the body, according to the National Institutes of Health.

(more)

Capsules (Cont'd)

Research Illustrated



The unusual reproductive habits of the ambrosia beetle make it a valuable genetic research animal. NIH-supported studies at the University of Wisconsin-Madison have shown that because the beetle can reproduce both sexually and asexually, each female is a potential species. While other insects reproduce in this fashion, the ambrosia beetle, officially called Xyleborus ferrugineus, *is the only such insect that has been raised successfully in test tube culture. Because all of the beetles within a single inbred colony have the same genetic makeup, the insects may be especially valuable in studies of DNA and RNA. In the photo, the male is the smaller of the two beetles. (NIH Photo #1133)*

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News Releases Issued

(Summaries of NIH releases sent out since the last issue. For a copy of any of these, please write or call.)

PULMONARY RESEARCH--The National Heart and Lung Institute is inviting young scientists and physicians to compete for grants to conduct pulmonary research in projects of their own design and direction. The new program--the "Young Investigator Pulmonary Research Grant"--is being launched this month. By providing them with modest independent support for projects of their own design, this program will help young scientists and physicians who are on the lower rungs of the professional ladder, while encouraging them toward pulmonary research, where new knowledge and diverse professional talents are greatly needed. Each applicant must be under 35, with a doctorate in some relevant field. Grant applications, which must be returned before December 1, and other information about this program may be obtained from:

Jay Moskowitz, Ph.D.
Acting Chief, Special Programs and Resources Branch
Division of Lung Diseases
National Heart and Lung Institute
Bethesda, Maryland 20014

#

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National Institutes of Health
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U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE ■ Public Health Service ■ National Institutes of Health ■ Office of Information ■ Bethesda, Maryland 20014

October 10, 1973

SPECIAL SUPPLEMENT: *NIH Portfolio on Stroke Research*

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NEWS & FEATURES From NIH October 10, 1973

Research Advances

TRACE ELEMENTS IN DIET AFFECT TOOTH DECAY RATE

A study of 21 elements in the fluoride-deficient drinking water of two isolated mountain villages in Colombia, South America, suggests that trace substances other than fluoride may account for one town having less than half as much tooth decay as the other.

In the two villages--Don Matias and Heliconia--the diet, climate, living conditions, age distribution, and racial stock are very similar. Neither village has more than an average level of 0.1 parts per million of fluoride in the drinking water, yet the relative amount of decay in groups of the same age was 13.9 in Don Matias, compared to only 5.5 decayed, missing, and filled permanent teeth in residents of Heliconia.

This study, designed to examine the concentration of trace metals in drinking water and to relate observed differences to the rates of prevalence of dental caries, was supported by the National Institute of Dental Research.

Investigators analyzed samples of drinking water from each village by emission spectroscopy, recorded the results photographically, and then compared the findings with known standards. As a result, they found that 13 of the trace elements studied were present in similar amounts in both towns. Titanium was higher in Don Matias, but not at a statistically significant level. However, the levels of copper, iron, and manganese were statistically higher in Don Matias where the higher decay rate is similar to that in much of South America and other low-fluoride areas such as Massachusetts. In contrast, the levels of calcium, magnesium, molybdenum, and vanadium were

(more)

significantly higher in Heliconia. These findings reveal clear-cut differences in exposure to trace metals from drinking water supplied in the presence of the same sub-optimal levels of fluoride.

The investigators point out that few studies of trace elements have ruled out completely a possible concurrent effect of fluoride. Nevertheless, some surveys indicate that hard water appears to be associated with reduced tooth decay in other parts of the world. Likewise, even more limited evidence suggests that excess copper and manganese may promote decay.

Decreased caries prevalence has long been inversely associated with hard water. However, the hardness of water is principally due to the presence of calcium and magnesium, although aluminum, iron, manganese, and other metals also contribute to the hardness. Therefore, associations with hard water may be statistical, while the direct causal association may be with one or more of the hardness components, while hardness itself may be secondary. Furthermore, reports on associations between caries prevalence and water hardness have failed to consider possible fluoride effects.

The investigators believe that while trace elements other than fluoride may exert pronounced effects on the prevalence of dental caries, considerable caution and more effort will be required before definitive causal relations may be established. Even more complex will be the evaluation of trace elements in the presence of significant levels of fluoride.

Previous spectroscopic analyses of soil samples in these towns showed somewhat similar local differences in the distribution of trace metals. However, dietary histories and studies of the sources of common foodstuffs

(more)

tend to support the hypothesis that any effect of trace elements is probably due to drinking water rather than to food.

The water analysis was reported in the September 1973 issue of *Archives of Oral Biology* by R.L. Glass, D.D.S., of the Forsyth Dental Center, Boston, Massachusetts; Kenneth J. Rothman, D.D.S., of the Harvard School of Public Health, Boston; Favio Espinal, D.D.S., and Herman Velez, D.D.S., of the University of Antioquia, Medellin, Colombia, South America; and N.J. Smith of the Dow Chemical Company, Midland, Michigan. A report of the soil analysis appeared previously in the *Journal of Dental Research*, November-December 1972.

#

Research Advances

20 Years of Research...

NIH SCIENTISTS LINK CANCER WITH BODY'S IMMUNE SYSTEM

A trail of research spanning nearly two decades has led to the discovery of a new link between cancer and the body's immune system.

Patients with a rare intestinal disease have been found to have an unique type of defect in their immune defense systems. The same patients have also been found to have an increased likelihood of developing cancer.

The immune defect is associated with a disease called intestinal lymphangiectasia, first described by physicians at the NIH Clinical Center. The disease is one of the protein-losing gastroenteropathies, a new class of diseases identified on the basis of studies started at the Clinical Center soon after it opened in 1953.

In patients with intestinal lymphangiectasia, the channels of the lymph system do not develop properly, particularly in the walls of the small intestine. The channels are larger than normal and allow the body fluid called lymph to leak into the small intestine and thus pass out of the body. This leakage of lymph causes a steady loss of white blood cells and dissolved proteins.

Thomas A. Waldmann, M.D., and co-workers at the National Cancer Institute (NCI) have found that patients with intestinal lymphangiectasia have a markedly depressed capability to carry out immune defense reactions. This is caused chiefly by shortages of lymphocytes. The NCI scientists discovered that lymphocytes in these patients are lost through their defective lymph vessels.

(more)

Cancer (Cont'd)

In addition, remaining lymphocytes have an impaired immune capability.

Cancer develops more frequently than normal in persons with various immune disorders and in transplant recipients who are given immunosuppressants to prevent rejection of donated organs. Cancer has also been found in an above-normal number of intestinal lymphangiectasia patients at the Clinical Center. This adds to the growing body of evidence on the importance of the immune system as a defense against cancer.

The loss of lymphocytes into the intestine represents another means by which the immune system can become defective. A number of other immune disorders have been identified by investigators at the Clinical Center and elsewhere. These disorders include decreased production of white blood cells and antibodies (proteins in the blood which neutralize bacteria and other harmful substances), destruction of antibodies by abnormal metabolic reactions, and defects in recognizing and attacking body invaders.

The growing understanding of intestinal lymphangiectasia emerged from nearly 20 years of work at the NIH Clinical Center. Scientists at several of the NIH Institutes studied patients with extremely low levels of protein in their blood. Over a period of years, Jesse L. Steinfeld, M.D. (later Surgeon-General of the Public Health Service); Robert Gordon, M.D., of the National Institute of Arthritis, Metabolism, and Digestive Diseases; Frederick Bartter, M.D., of the National Heart and Lung Institute; Warren Strober, M.D., of the National Cancer Institute; and other NIH scientists identified in these patients a new class of diseases, the protein-losing gastroenteropathies, in which proteins from the blood were lost into the

(more)

Cancer (Cont'd)

gastrointestinal tract. As understanding of this disorder progressed, several new diseases were discovered, including intestinal lymphangiectasia. More than 90 diseases are now associated with protein-losing gastroenteropathy.

Dr. Waldmann has been studying protein-losing gastroenteropathy and diseases with immune defects since joining NCI and the Clinical Center staff in 1956. He reported on the study of intestinal lymphangiectasia at a recent convocation celebrating the Clinical Center's 20th anniversary, July 1973.

#

Research Advances

IN THE LITERATURE:
Transplantation, May 1973

FETAL TISSUE TRANSPLANTS FAIL TO RECONSTITUTE IMMUNE SYSTEM--Fetal thymus and liver tissue transplants do not offer much hope for treating children born with serious immune deficiencies, according to a team of American and English doctors who have reported their experience with four young patients.

The scientists, partially supported by the National Institute of Allergy and Infectious Diseases (NIAID), found no evidence of the establishment of either humoral (production of circulating antibodies) or cellular immunity in any of the children following transplant and prior to their deaths from overwhelming infections.

These negative findings confirm the lack of success reported previously by other investigators whose studies were not as carefully controlled.

Marrow transplants from a sibling whose tissue antigens match those of the patient have been successful in a number of children with immunological deficiencies. However, in many cases there is no suitable sibling donor. Encouraged by the results of animal studies, investigators have hoped that, by using immunologically immature fetal tissue, unmatched donors could be used without the risk of a graft-versus-host reaction in the recipient. Children born without the capacity to make antibodies or mount a cell-mediated response to antigens readily accept incompatible grafts since they lack the ability to reject them immunologically; but, if the graft does not "match," it is likely to attack the body itself.

(more)

Transplants (Cont'd)

In the present study, the investigators found no evidence of a graft-versus-host reaction in any of the patients, but, of course, there was no immunological activity either.

In discussing reasons why the fetal transplants failed, the scientists point out that the causes of genetically acquired immunological deficiencies remain unknown. More may be involved than an abnormality in thymus development; there may also be a deficiency of some factor necessary for stimulation of immunological maturation. Or, factors may be produced which interfere with the development of immunocompetence. The investigators speculate that at some time in the future it may be possible to use the immunologically mature tissue of incompatible donors if specific tolerance to the recipient's cells can be achieved in the graft.

Identification of tissue (HL-A) antigens was carried out in one case after several transplants had been attempted. Tissue typing revealed either that some of the transplants had "taken" (but without demonstrable immunologic activity) or that the patient's own white cells had on their surfaces a bizarre array of HL-A antigens.

The transplant operations were performed by NIAID grantees and others at the University of Colorado's General Clinical Research Center, Denver--an institution funded by NIH's Division of Research Resources. Tissue typing was carried out by NIAID grantees at the University of California, Los Angeles. Much of the fetal tissue was flown to Denver from a London hospital where it had been obtained following spontaneous or therapeutic abortion.

(more)

Transplants (Cont'd)

Authors of the report which appeared in the May 1973 *Transplantation* were: J.H. Githens, V.A. Fulginiti, V. Suvatte, G. Schroter, W.E. Hathaway, D.S. Pearlman, H.E.M. Kay, P.I. Terasaki, G.J. Hill, C.H. Kempe, and S.T. Cox.

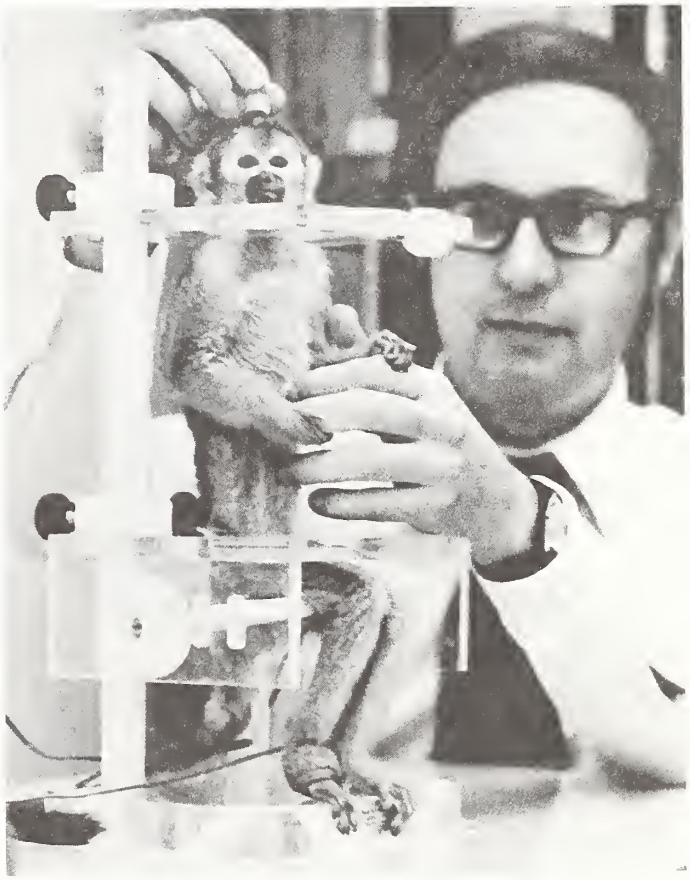
#

Photo Feature

TEXAS INVESTIGATOR SEEKS CLUES TO BODY TEMPERATURE REGULATION

Among the many mysteries surrounding man is how the human body regulates temperature. When we get hot, what makes us sweat? When we have a fever, what keeps it within bounds? And when we develop a bad case of heat stroke, what went wrong? What happens when a fever breaks out of human limitation and the end result is death?

James M. Lipton, Ph.D., assistant professor in both the Department of Physiology and the Division of Psychology at the University of Texas Southwestern Medical School at Dallas, is studying heat regulation. His work is supported by the National Institute of Neurological Diseases and Stroke.



Dr. James M. Lipton adjusts the brain implant used in a temperature regulation study. He is looking for the particular body mechanism that controls fever in squirrel monkeys. (NIH Photo #1134)

Dr. Lipton has underway a number of temperature regulation experiments with squirrel monkeys. He is looking for the particular body mechanism that mediates fever, and also testing a theory that newly-discovered "super hormones"--prostaglandins--have something to do with this process. It is hoped that gaining

(more)

knowledge in this area might lead the physician to better ways of handling high fevers and the convulsions which sometimes accompany them.

Dr. Lipton is investigating the effects of various drugs on the body temperature of rats. He uses a heat lamp on white rats restrained in jars. A rat can turn the lamp off by pressing a lever when the heat becomes uncomfortable.

After one of Dr. Lipton's rats (left) becomes uncomfortable from the heat generated from the light, it pushes the lever (right) to turn the light off. (NIH Photos #1135, 1136)

Once Dr. Lipton determines the rat's discomfort rate, he injects the animal with various drugs, including aspirin. Dr. Lipton has discovered that aspirin causes the rats to push the levers more often, indicating they are less tolerant of heat after taking this common drug.

#

News Feature

NIH SUPPORTS EXTENSIVE RESEARCH ABOUT STROKES

Few Americans do not know a family that has experienced the tragedy of a stroke. The families of some 500,000 Americans have first-hand experience with it each year. In too many of these instances, the physician has to explain that beyond close surveillance for complications and supportive care, there is very little he can do. Surgery is seldom possible, and the prescribing of drugs is uncertain at best.

With all the miracles of modern medicine, the prevailing attitude relating to stroke among physicians as well as laymen is still one of helplessness. The belief that this can be changed has led to a vigorous and highly promising stroke research program at the National Institute of Neurological Diseases and Stroke (NINDS).

The term "stroke" refers to a sudden loss of brain function resulting from interference with the blood supply to the brain. Strokes range in severity from minor episodes with transient neurological deficit to those causing death within a few minutes. Usually, strokes are brought on by one of three events: thrombosis (a local clot within a blood vessel in the neck or in the brain); cerebral embolism (the blocking of a blood vessel in the brain by a clot carried from some other part of the body); or hemorrhage (the rupture of a cerebral blood vessel).

All brain cells require oxygen and glucose and they receive their supply entirely from the blood stream. The need for an adequate blood supply to the brain can be seen from the fact that although the brain comprises

(more)

only two percent of the total body weight, it normally uses 20 percent of the body's total oxygen supply. Brain tissue cannot store oxygen, and therefore is completely dependent from minute to minute on an adequate flow of blood. When brain tissue is deprived of oxygen for more than four or five minutes, nerve cells stop functioning and may begin to die, and temporary or permanent paralysis of movement, thought, speech, or sensation is the result. When one adds to this almost impossible time factor the delicacy and relative inaccessibility of the brain, it is easy to see why a stroke creates such a feeling of helplessness on the part of the physician.

In spite of the obstacles, scientists and physicians working under the NINDS program have reasoned that some useful measures can now be taken, and that through research, new measures can be devised. Some strokes are preceded by headaches, vision, or speech problems, numbness, and other warning signs. Possibly these strokes could be prevented.

Medical statisticians have shown that people with any degree of high blood pressure have more strokes. If more could be learned about this and other causes of strokes, prevention could become even more important. If more were known about the dynamics of blood flow in the brain, and the chemical metabolism of brain cells, perhaps the damage done by a stroke could be reduced, confined, or even averted by quick treatment.

The essential elements of NINDS' stroke program are: (1) a group of grant-supported cerebrovascular research centers; (2) a group of about 50 research project grants; and (3) a new program of "Stroke Acute Care Research Units." The Institute has also begun a small intramural research program in

Bethesda, Maryland, concerned at first with cerebrovascular disease in persons under 40.

The cerebrovascular research centers, located in large university medical complexes across the country, make up the largest segment of the program. These units are staffed by as many as 15 to 20 scientists and physicians, plus technicians and other assistants. Some concentrate on single research areas, such as epidemiology and statistics or aphasia; others encompass several approaches, such as cerebral blood flow, brain metabolism, pharmacology, surgery, development of new diagnostic devices and techniques, and others. Generally, the centers have interrelated clinical and basic research programs, and some have accommodations for as many as 30 patients. Most also conduct training programs for young physicians, scientists, and other staff members.

In addition to these large team efforts, other research projects are continuing to contribute new knowledge to the field. They range from basic laboratory studies in such fields as neurophysiology and biochemistry to studies of the effects of drugs and the success of new surgical techniques in patients. Informal training is provided on many of these projects.

Since 70 to 80 percent of stroke mortality occurs within the first 10 days, and since the outlook for survivors depends heavily on the quality of care during the acute phase of the crisis, the need for better "acute care" is urgent. In March 1973, the Department of Health, Education, and Welfare funded new acute care research units in 10 university medical centers. These units will be especially equipped for research studies, and in some

(more)

cases, round-the-clock monitoring. They will resemble the intensive care units that have been so successful in managing coronary disease, except that they will be oriented toward research on the brain, so that better methods can be developed for care of the stroke patient. They will also provide a vital training resource for physicians, interns, and ancillary personnel.

#

NOTE TO SUBSCRIBERS: For information and photos about the NINDS-supported stroke research centers, please see the special supplement to this issue of NFFN, *the NIH Portfolio on Stroke Research.*

Photo Feature

RATS RIDE BICYCLES TO STRENGTHEN BONES

Ali Seireg, Ph.D., a mechanical engineer at the University of Wisconsin-Madison, exercises rats in a bicycle-like device which causes the rat to pedal with one leg in two-second cycles against a force roughly equivalent to its body weight while holding the other leg still.

Analyzing the bones of rats subjected to the exercise programs, Dr.Seireg has found that frequency and magnitude of stress applied to the leg changes bone size and mineral content and, therefore, strength.

His research concerning the effects of stress on bone mineral content, the role of muscle fatigue in fracture, and the causes of wear in joints is supported by the National Institute of Arthritis, Metabolism, and Digestive Diseases.

"It's well known that you can make any muscle stronger by exercising it," Dr. Seireg points out. "We're now starting to realize the importance of exercise to bone strength as well."

But the strength of the bone itself isn't the whole story. Dr. Seireg has also measured how the frequency of an applied load will affect how much of a load is needed to break a bone.

"The muscles and the bone work together," Dr. Seireg continues. "Soldiers on long hikes often get what is called 'march fatigue,' which involves cracks in the leg bones, because the muscles get too tired to provide adequate support."

An overload of exercise also leads to damage in the joints. Like bones, cartilage increases in mineral content when it is under stress.

(more)

BICYCLES (Cont'd)

Dr. Seireg explains that cartilage is elastic enough to distribute stress evenly in the joint. However, as exercise calcifies the cartilage, the joint stiffens and the stress distribution becomes uneven, making the cartilage corrode faster."

Breakdown of synovial fluid, the lubricant in joints, also causes cartilage to become worn.

According to Dr. Seireg, "With too much exercise, the body cannot rejuvenate the synovial fluid fast enough. As the fluid breaks down like overheated crankcase oil, the temperature in the joint rises.

"Joint temperature may actually prove a good tool for measuring damage in living animal joints," he predicts. "This and the other techniques we have developed provide a tool for testing drugs and methods of treatment to avoid arthritis that comes from stress."

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Ali Seireg, Ph.D., straps a rat into a bicycle-like device to study bone and joint conditions. (NIH Photo #1137)

Medical News Tip

HEARING, SPEECH, AND LANGUAGE--Early in 1973, a new section in Collaborative and Field Research, National Institute of Neurological Diseases and Stroke (NINDS), was established to develop and coordinate a directed research program to improve the outlook for people afflicted with communicative and other sensory disorders. Research projects in this section include Infant Hearing Health, Hearing Aid Tailoring, and Cross-modality Sensory Aids.

Inner ear deafness and early detection of deafness are also among the important problems under investigation at the clinical research centers supported by NINDS in the area of communicative disorders.

Many young people, as well as many people in the over-65 age group, are excluded from normal living because of hearing and speech disabilities. Therefore, prevention, early detection, treatment, and improved aids are imperative in the young with extensive hearing loss if they are to develop speech and language and be educated in regular classes. Effective treatment and improved aids are also important to older citizens.

For additional information about NINDS studies of hearing, speech, and language, contact: NINDS Information Office, Bldg. 31, Room 8A-03, NIH, Bethesda, MD 20014, Phone (301) 496-5751.

#

Capsules

Factual Fillers

SKIN CANCER--Skin cancer is the form of cancer that occurs most often among Americans, reports the National Institutes of Health. Fortunately, it is 95 percent curable by surgery or irradiation. For many patients, radiotherapy is the treatment of choice because it may destroy cancerous tissue with little damage to surrounding areas and overall appearance. Low-voltage radiotherapy is useful for small superficial skin cancers.

MYASTHENIA GRAVIS--Myasthenia gravis attacks the point at which nerve meets muscle, stopping the electrical impulse before it can excite the muscle to contract, reports the National Institutes of Health. The disease can be effectively controlled in many cases, but without treatment it becomes progressively worse.

TIC DOULOUREUX--One of the most agonizing pains of man is caused by the affliction of the face known as trigeminal neuralgia or tic douloureux. These spasmodic nerve pains of the jaw usually attack people over 40, and can be debilitating in their effects, reports the National Institutes of Health.

TRIGEMINAL NEURALGIA--Trigeminal neuralgia is one of the most common of all neuralgias, reports the National Institutes of Health. Although its exact cause is not known, its symptoms often arise in connection with infections of the teeth or nasal sinuses. Occasionally, this neuralgia is associated with tumors or other disorders of the nervous system.

Capsules (Cont'd)

RADIATION THERAPY--Certain bone tumors have been shown curable by radiation therapy without the necessity of surgical amputation, reports the National Institutes of Health. The most promising new studies have concerned Ewing's sarcoma, a usually fatal form of bone cancer occurring among children and young adults.

HISTOPLASMOSIS--The most common fungal lung disease, histoplasmosis, is caused by an organism *Histoplasma capsulatum*. An estimated 30 million Americans are infected with it, reports the National Institutes of Health. The spores of this fungus thrive in soil enriched by bird droppings.

FEVER BLISTER--No drug will cure a fever blister, reports the National Institutes of Health. However, dentists and physicians can make patients more comfortable by prescribing local anesthetics to relieve pain, ointments to soften crusts, or antibiotics to control secondary bacterial infections which may invade the open sores.

COLD SORES--Blisters which form along the outer edge of the lips or under the nostrils are commonly called cold sores or fever blisters because years of observation have shown that they often accompany respiratory infections or some other temperature disturbance such as sunburn, reports the National Institutes of Health.

TOOTH LOSS--Periodontal (gum) diseases cause most of the loss of teeth in adults, reports the National Institutes of Health.

(more)

Capsules (Cont'd)

Research Illustrated

Each heart beat sends a pulse of blood into the dental pulp of a living tooth. To determine if a tooth is alive, National Institute of Dental Research scientists have used transillumination. This nondestructive technique involves a narrow, controlled beam of light directed from a bundle of optical fibers through a tooth and into a second bundle of fibers.
(NIH Photo #1138)

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New Publication:
The Relationships Between Speech and Reading

A new publication, *The Relationships Between Speech and Reading*, by Ignatius G. Mattingly and James F. Kavanagh, has been adapted by the National Institute of Child Health and Human Development (NICHD) from an article in *The Linguistic Reporter*, October 1972.

In the booklet, which deals with the differences between the spoken and written language, the authors conclude that reading is not a primary linguistic activity but a secondary language-based skill requiring a degree of linguistic awareness. The form in which a written sentence presents itself to the reader is determined not by the actual information to be conveyed by the sentence but by the writer's linguistic awareness of the process of synthesizing the sentence, an awareness which he wishes to impart to the reader.

Since the reader has much the same linguistic awareness as the writer, and is familiar with the conventions of the writing system, he can synthesize something approximating what the writer intended, and so understand the sentence.

Science writers can obtain a free copy of this publication from:

NICHD Information Office
Landow Building, Room A804
Bethesda, MD 20014
Phone (301) 496-5133

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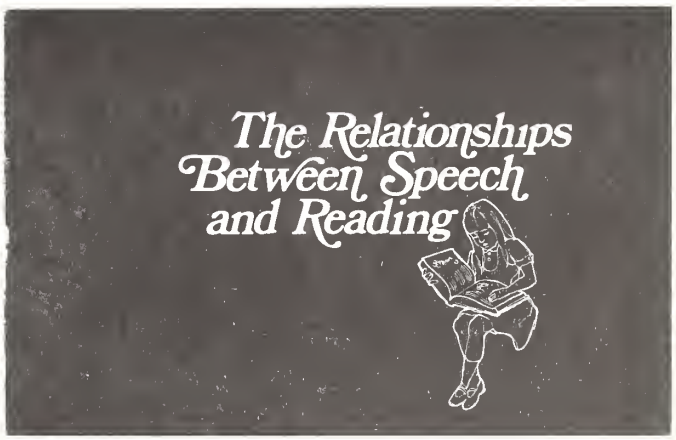

News Releases Issued

(Summaries of NIH releases sent out since the last issue. For a copy of any of these, please write or call.)

MELANOMA--A drug proven to be helpful in treating malignant melanoma, a fatal form of skin cancer, will be manufactured and made available under an agreement between the National Cancer Institute (NCI) and Miles Laboratories, Inc., Elkhart, Indiana. The drug, called DTIC, dacarbazine, or imidazole carboximide, is useful in advanced stages of melanoma when this rare form of skin cancer is no longer curable by surgery. In NCI-sponsored studies, approximately 20 percent of more than 700 patients with advanced melanoma responded to DTIC with disappearance or lessening of the disease for at least four weeks. Several other drugs have given comparable response rates in some studies, but the responses with DTIC have been more consistent in the NCI tests.

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PORTFOLIO

STROKE RESEARCH

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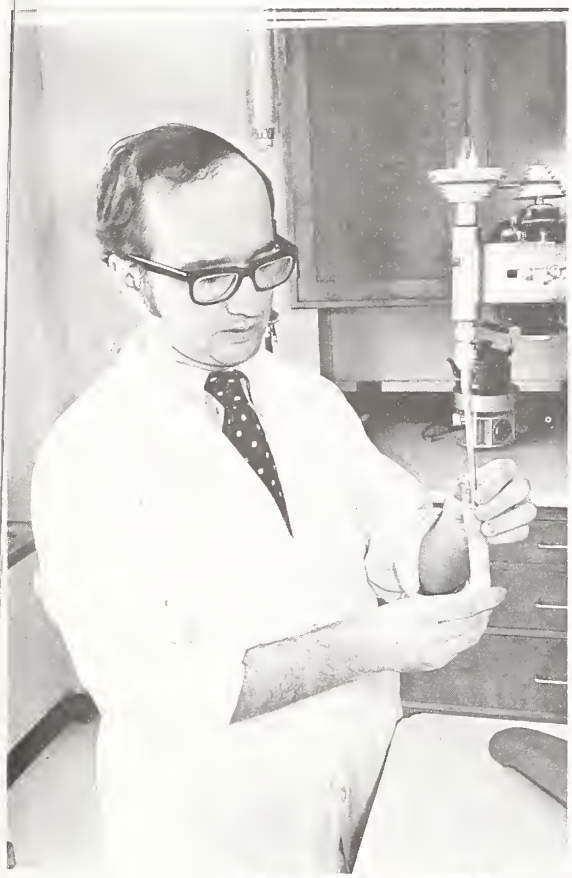

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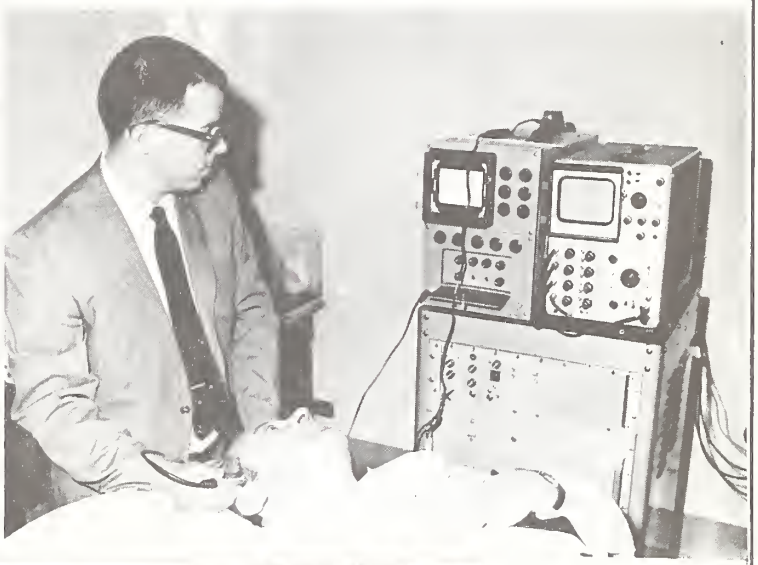

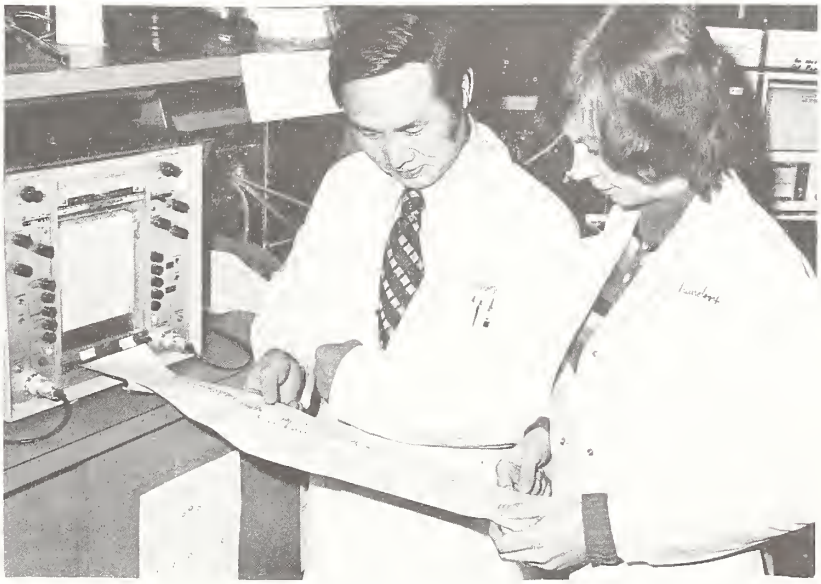

NEWS&FEATURES FROM NIH

NIH PORTFOLIO ON STROKE RESEARCH....OCTOBER 1973

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE ■ Public Health Service ■ National Institutes of Health ■ Office of Information ■ Bethesda, Maryland 20014

Marc Stern, Editor
Carol M. Sussman, Associate Editor
NIH News Branch, Building 31, Room 2B-10, Bethesda, MD 20014, [301] 496-1206

INTRODUCTION: NINDS STUDIES CAUSE, CONTROL OF STROKES

This introduction was prepared with the assistance of Donald B. Tower, M.D., Ph.D., acting director of the National Institute of Neurological Diseases and Stroke (NINDS). Dr. Tower, who headed the NINDS laboratory of neurochemistry before assuming his present post, has contributed significantly to the understanding of the brain with his many articles on brain metabolism and physiology. NINDS is a component of the National Institutes of Health, an agency of the U. S. Department of Health, Education, and Welfare.

Stroke, or cerebrovascular accident, kills nearly 200,000 Americans every year and incapacitates an additional 300,000. The survivors join the two million Americans living today who have suffered one or more strokes.

More than 10 years ago, the National Institute of Neurological Diseases and Stroke (NINDS) recognized the importance of multidisciplinary research in seeking causes and controls for stroke. In 1962, the Institute initiated a special program to establish a network of cerebrovascular research centers in leading universities and hospitals across the country. Today, there are 10 stroke research centers serving as regional focal points to study the prevalence, cause, and treatment of stroke.

At these centers, teams of basic science investigators and research clinicians are working together to uncover new information about stroke and translate it as fast as possible into clinical service.

A stroke occurs when an artery to a portion of the brain ruptures or becomes blocked as a result of thrombosis (a clot which forms in a blood vessel) or embolism (a clot brought from another blood vessel).

(more)

While approximately 36 percent of those who suffer a stroke die, the majority live for months or years after stroke. About 30 percent of the survivors recover adequately to resume their previous work or life style. However, they continue to run a high risk for subsequent strokes. An additional 15 percent are made totally dependent by stroke and face institutional care for life. The remainder, approximately 55 percent, survive with lifelong motor, sensory, or mental disabilities which preclude work and limit recreation.

Despite the giant strides already taken in the fight against stroke, the mortality from this disorder has remained unchanged for many years. However, researchers are hopeful that stroke can be prevented. Recent studies have identified significant factors leading to stroke: high blood pressure, heart disease, atherosclerosis (the buildup of fatty plaques inside the artery walls), and advancing age individually and cumulatively increase the risk of stroke.

Studies on the geographic distribution and the natural history of stroke, which are being conducted at several of the stroke research centers, may give important clues about other factors that may contribute to stroke and that may be controllable.

Every stroke is associated with disturbances of cerebral circulation which results in areas of reduced blood flow (ischemia) of varying magnitude. One of the most serious complications of a stroke is cerebral edema, the collection of fluid in the brain. The basic studies on cerebral ischemia and edema underway at several research centers are crucial for the development of successful management of stroke. By understanding the mechanisms by which brain damage occurs in stroke, it may be possible to design measures to prevent the spread of injury and facilitate recovery of partially destroyed regions of the brain.

Advances in microvascular surgical techniques offer new hope to patients whose ischemic injury has not yet reached the point of irreversibility.

Over a relatively short period, investigators at these centers have been able to provide answers to many important questions relating to the control and management of stroke. In any research effort, however, one answer often generates many new questions. The central role of hypertension in stroke, for example, has been well established. However, discovery of the mechanism by which the brain controls blood pressure to all parts of the body would lead to improved drugs for control of hypertension and lead to a primary prevention of stroke.

Scientists are hopeful that basic research of brain metabolism will identify the chemical changes that signal irreversible damage and the mechanism through which imminent brain damage may be reversed.

By evaluating the results of intensive care in acute stroke, investigators may be able to develop techniques to save more lives and reduce damage resulting from stroke.

Exploration into the potentials of rehabilitation will afford more patients the opportunities to live independently after stroke.

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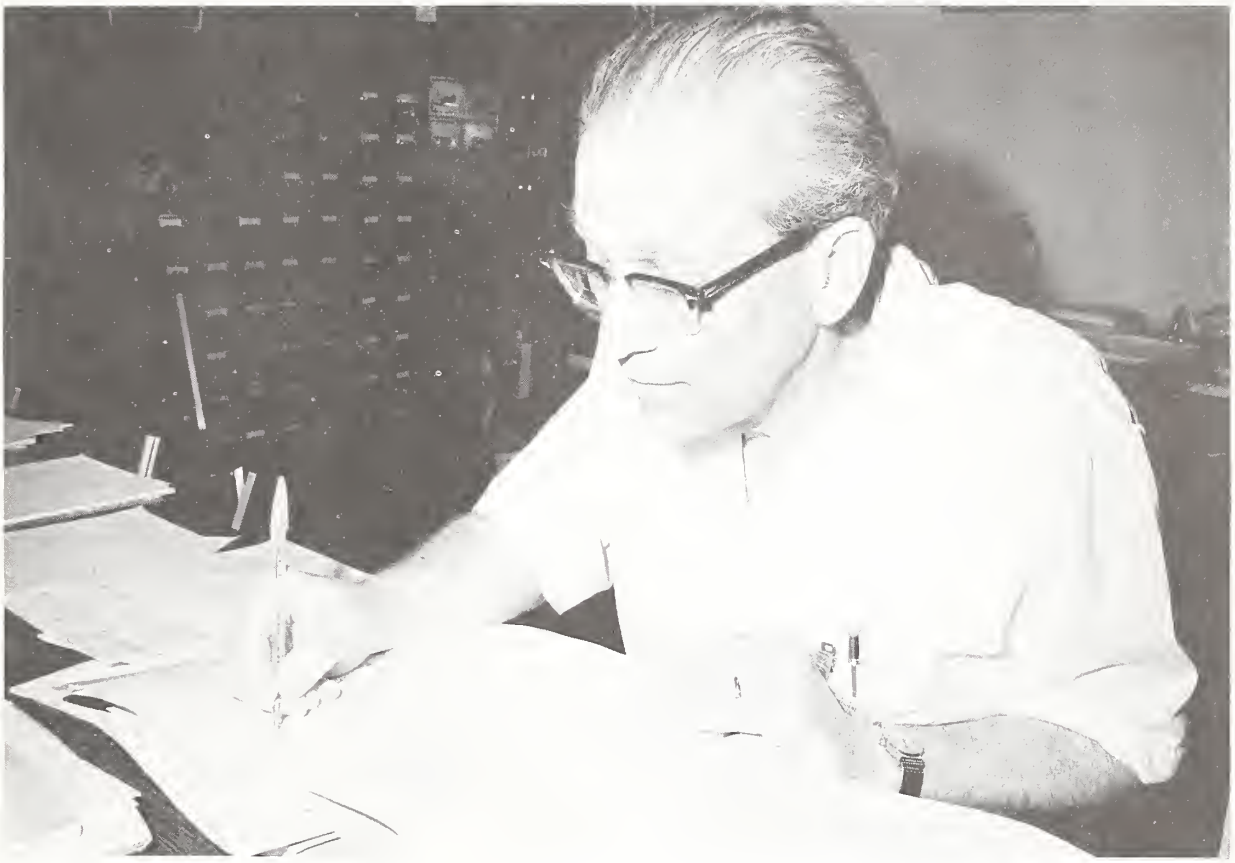
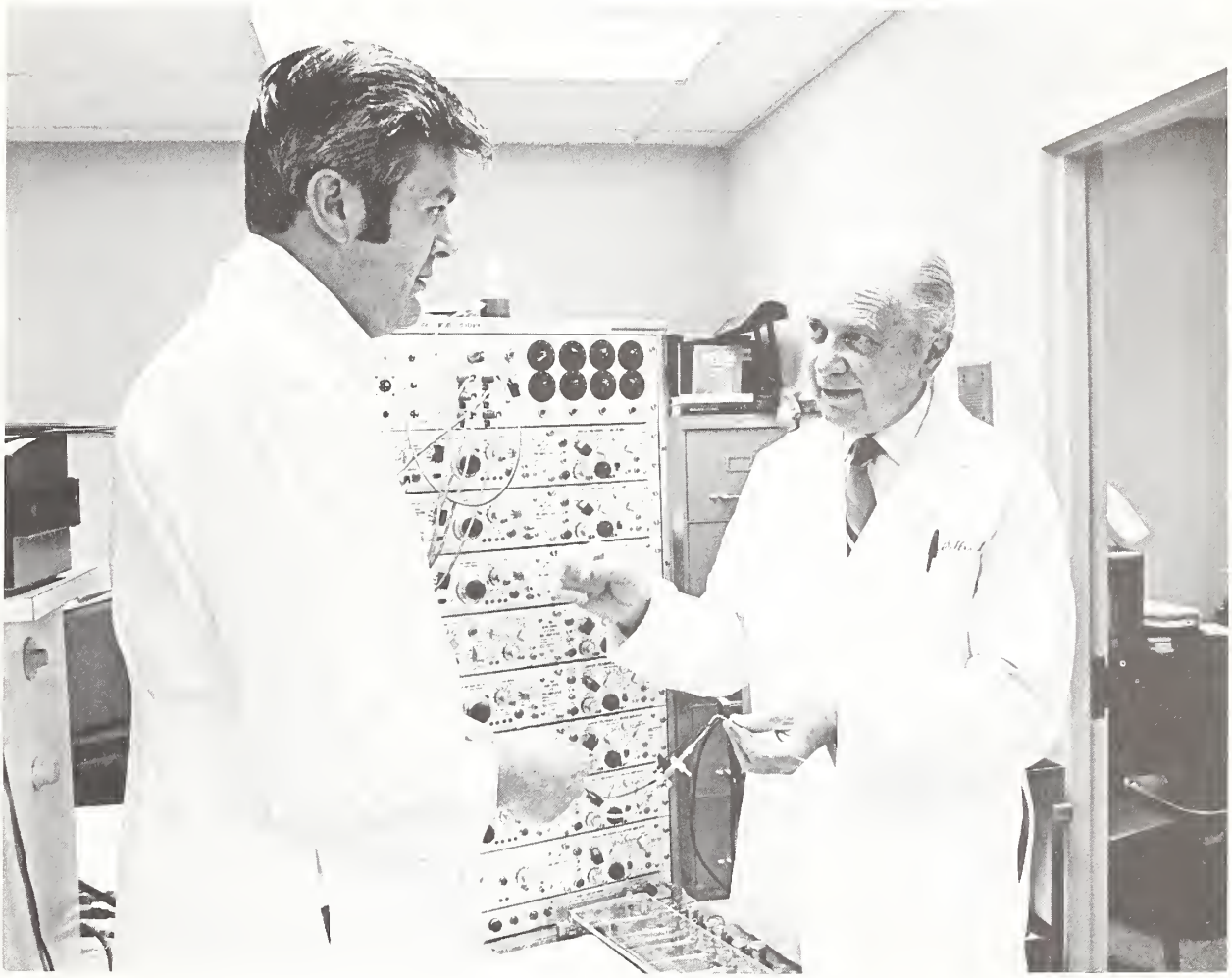
Murray Goldstein, D.O., associate director for Extramural Programs, NINDS, has been the NIH official with overall responsibility for the development of the cerebrovascular grant program. He has been a leader in coordinating the efforts of the centers, and in providing administrative support from the Institute.



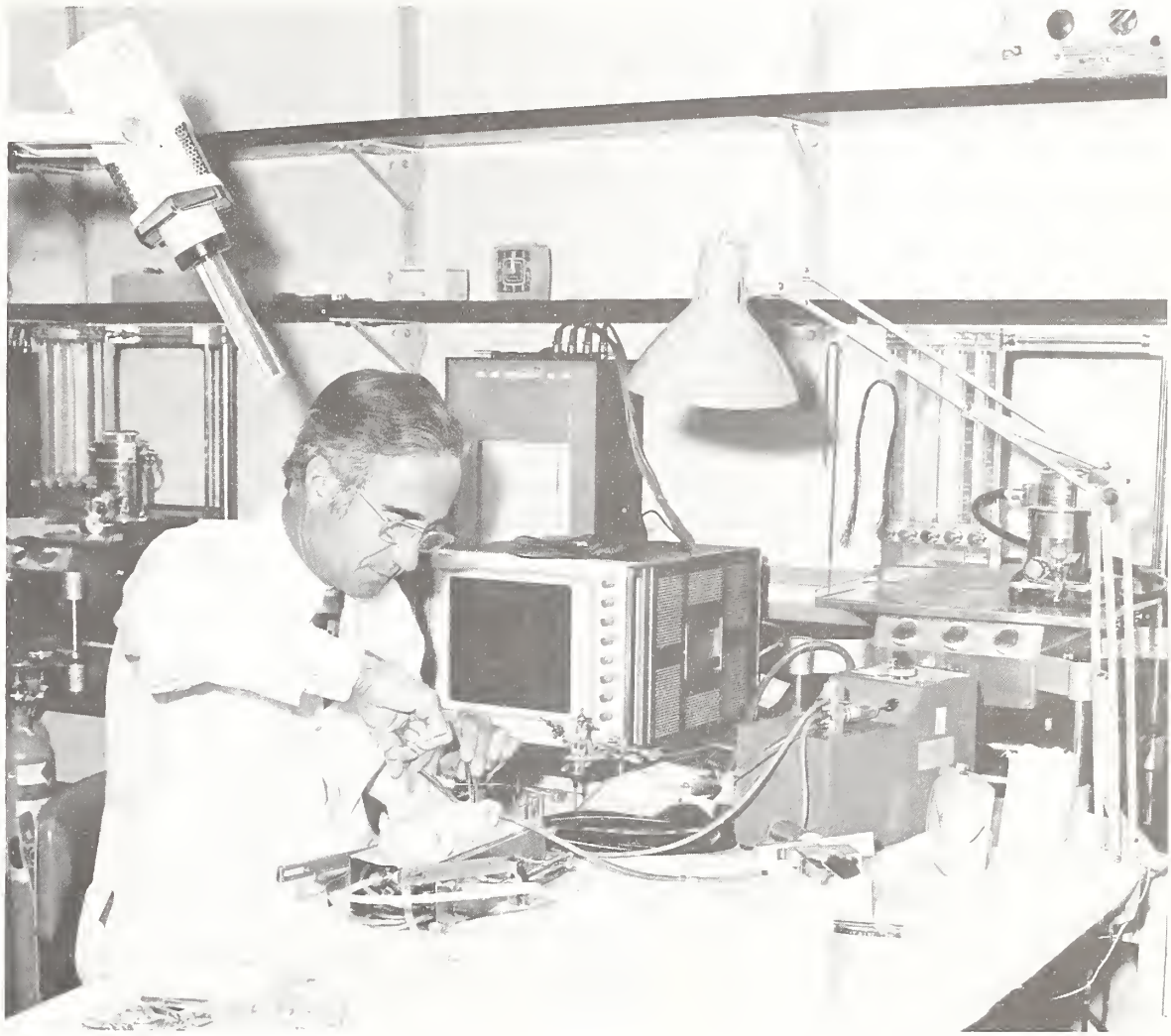
BALTIMORE, MD--Abraham Lilienfeld, M.D., chairman of the Department of Epidemiology at Johns Hopkins University, examines a computer printout of the factors which might increase the risk of stroke. Dr. Lilienfeld is the principal investigator in a study supported by the National Institute of Neurological Diseases and Stroke. Dr. Lilienfeld and his team of researchers have identified areas in the United States which have abnormally high incidences of stroke and are comparing persons living in these areas with persons living in areas with an unusually low incidence. By administering complete physical examinations to a randomly chosen segment of the population in these high and low areas, Dr. Lilienfeld and his co-researchers hope to identify factors which increase the risk of stroke and factors which favor avoiding stroke. The results of this research may greatly help physicians better understand the causes of stroke and aid in preventing its occurrence. (NIH Photo #ST-1)

BALTIMORE, MD--Erland Nelson, M.D., chairman of the Department of Neurology at the University of Maryland School of Medicine, is shown with an electron microscope used in scanning the surface of blood vessels in the brain. Dr. Nelson is investigating the problems of cerebral blood flow and arteriosclerosis through a Stroke Research Center supported by the National Institute of Neurological Diseases and Stroke. Investigators at the Center are also examining new methods for monitoring cardio-respiratory interaction as a means of better clinical assessment and therapy in stroke patients. (NIH Photo #ST-2)



BIRMINGHAM, AL--J. Garber Galbraith, M.D., (right) director of the Division of Neurosurgery at the University of Alabama, and Ed Strong, a laboratory monitoring technician, discuss the use of a Grass Recorder used to measure the oxygen supply in the brain. This technique is useful to the physician because it helps him evaluate the effectiveness of various treatments by measuring the amount of oxygen reaching the brain after treatment. This is one of many procedures used by physicians at the Cerebrovascular Research Center to better understand the most effective means of treating stroke patients. The Research Center is supported by the National Institute of Neurological Diseases and Stroke. (NIH Photo #ST-3)

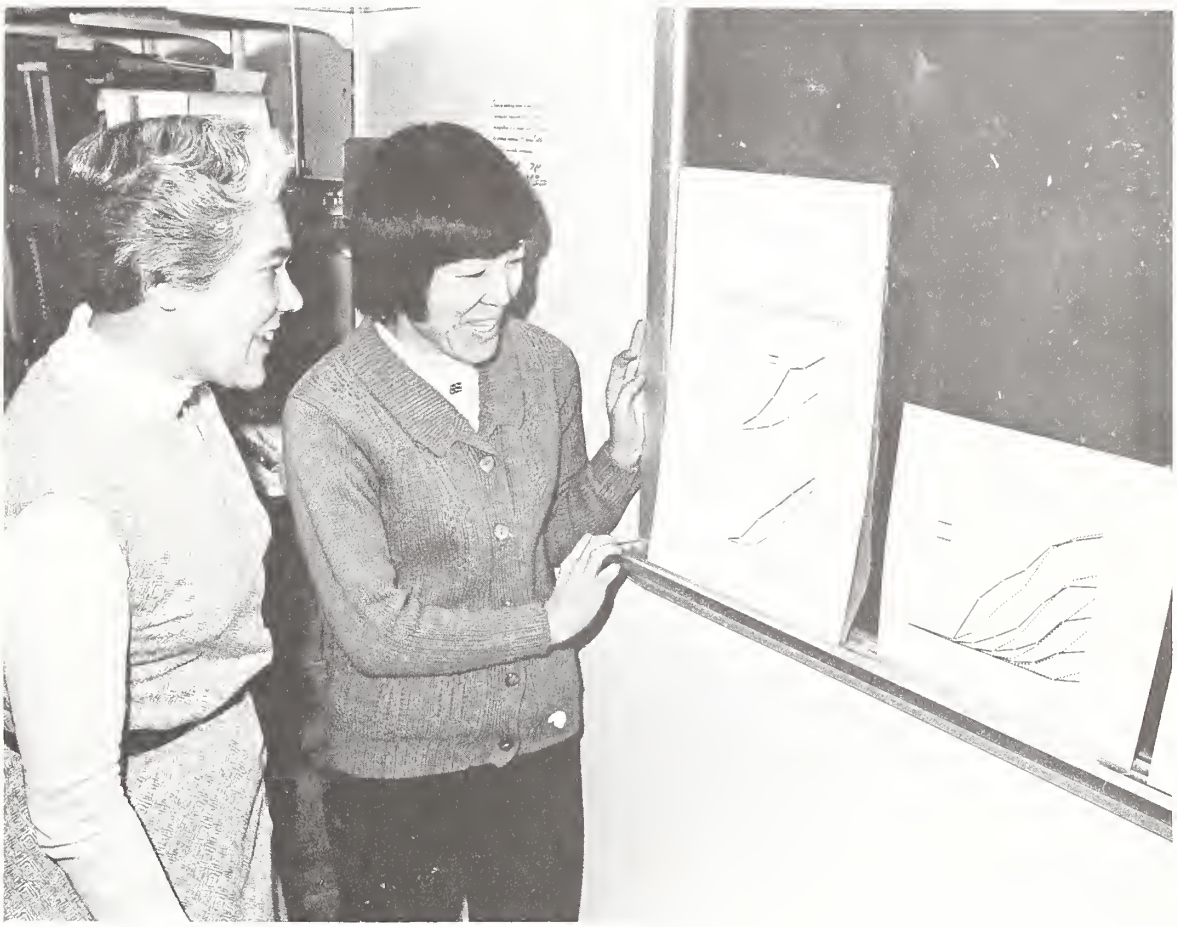
BOSTON, MA--Harold Goodglass, Ph.D., director of the Boston University Aphasia Research Center, is shown speaking to an aphasic patient. Aphasia is a speech disorder resulting from brain damage often caused by stroke. The Center, which has made important contributions in the study of aphasia, phycholinguistics, and neuropsychology, is unique in its ability to answer important questions in the field of language disorders. Investigators currently are developing automatic programmed retraining methods for aphasics and are refining tests to improve clinical diagnosis. The Boston University project is funded by the National Institute of Neurological Diseases and Stroke. (NIH Photo #ST-4)



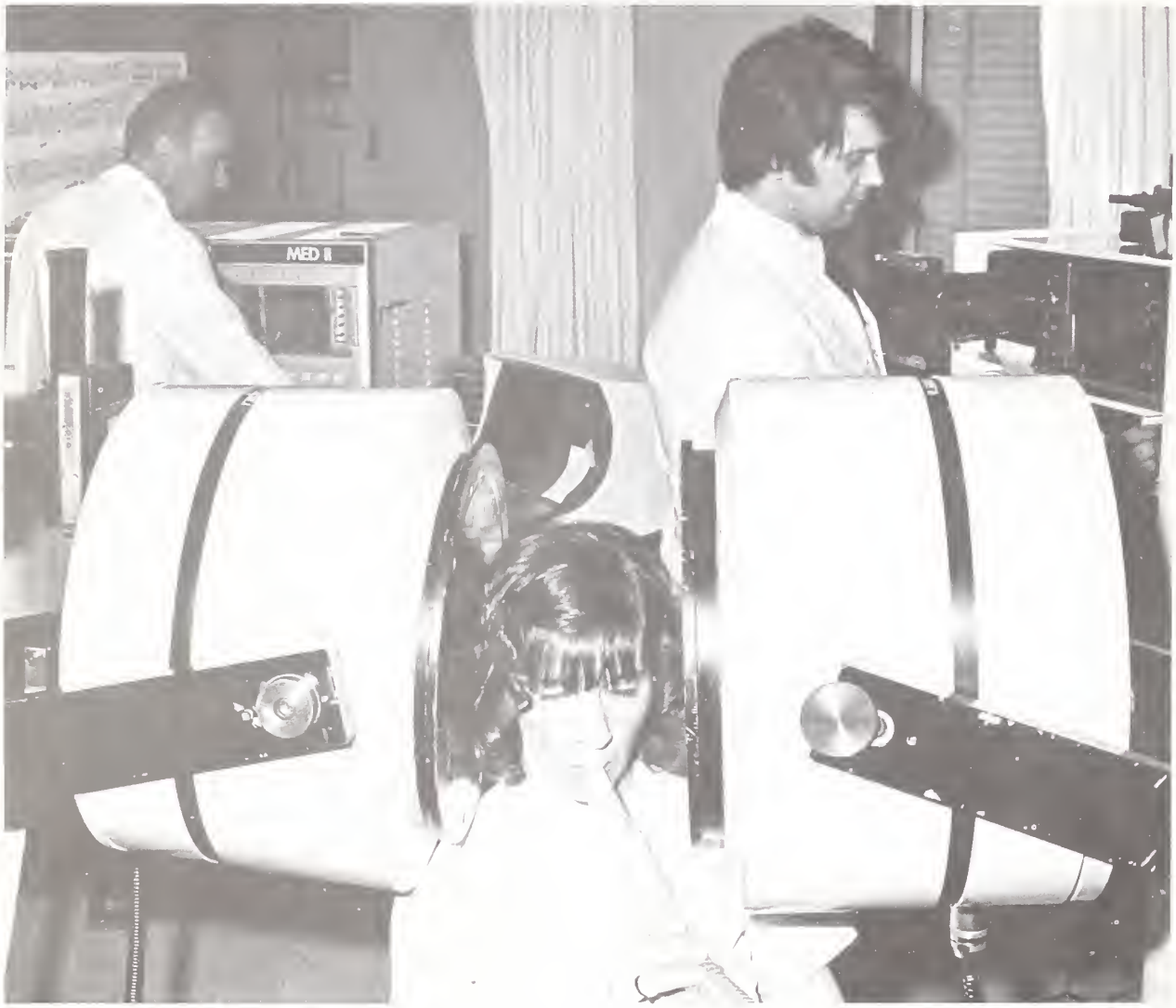
MIAMI, FL--Peritz Scheinberg, M.D., chairman of the Department of Neurology at the University of Miami, is shown preparing a rat for cerebral metabolic studies. Dr. Scheinberg works with a team of researchers in the Cerebrovascular Research Center supported by the National Institute of Neurological Diseases and Stroke. Through their research, the investigators hope to learn more about mechanisms of recovery, phenomenology, natural history, and pathology of stroke. They are also working on more effective methods of measuring the flow of blood in the brain. (NIH Photo #ST-5)

MINNEAPOLIS, MN--Abe B. Baker, M.D. (left), head of the Department of Neurology at the University of Minnesota Medical Center, coordinates and directs the Cerebral Vascular Research Center supported by the National Institute of Neurological Diseases and Stroke. The research center has two main areas of emphasis: (1) clinical studies of the natural history of stroke, and (2) the causative factors and geographical distribution of atherosclerosis in the major blood vessels of the brain. The center has been under Dr. Baker's direction since its beginning in 1961 and has made significant contributions to the understanding of the basic causes and distribution of stroke. (NIH Photo #ST-6)

MINNEAPOLIS, MN--Arthur Klausen, M.D. (right), director of the Intensive Care Unit (ICU) at the University of Minnesota Medical Center, examines a printout from an Impedance Pneumograph--a device which shows the patient's respiratory rate and pattern. Physicians in the ICU can monitor a patient's respiration, heart activity, and brain activity to gain instantaneous information on a critically ill patient's vital functions. The complete diagnostic and treatment facilities available in the ICU aid researchers in finding the most effective means of treating stroke patients. The comprehensive facilities in the ICU also allow top level care of stroke patients and provide training for physicians and nurses in the evaluation and care of the critically ill stroke patient. The research aspects of the intensive care unit are supported by the National Institute of Neurological Diseases and Stroke. (NIH Photo #ST-7)



MINNEAPOLIS, MN--Ruth Loewnson, Ph.D. and Mary Bilek, staff statisticians at the University of Minnesota Medical Center, examine graphs showing the incidence of cerebral atherosclerosis at different ages. These graphs are a small part of a major study of the geographical distribution of cerebral atherosclerosis being conducted at the Stroke Research Center at the University of Minnesota. The study is a world-wide undertaking in which cooperating researchers from many nations send brain sections to the Minnesota researchers for evaluation of the amount of fatty plaque in arteries of the brain. By collecting these data, the Minnesota researchers hope to provide information on the effect of diet and other factors on increased risk of stroke. This research is supported by the National Institute of Neurological Diseases and Stroke. (NIH Photo #ST-8)



MINNEAPOLIS, MN--Merle Loken, M.D., (left) head of the Division of Nuclear Medicine, and Jim Tennison, nuclear medicine technician, examine the flow of blood in a model patient's head to assess brain damage from a stroke. The patient inhales xenon gas which enters the blood stream, flows to the brain, and is detected by two gamma cameras, one on either side of the patient's head. The cameras sense the presence of the gas in the blood vessels of the brain. Dr. Loken can then assess the severity of the stroke by seeing what portions of the brain are damaged and to what extent. This feat of medical wizardry applies a variety of sophisticated technology including complex computers to analyze the data. Through the use of this technique, physicians can assess both the patient's needs and the benefit of treatment. The stroke research effort at the University of Minnesota is supported by the National Institute of Neurological Diseases and Stroke. (NIH Photo #ST-9)

PHILADELPHIA, PA--Investigators participating in an NINDS-supported Stroke Research Program at the Philadelphia General Hospital Stroke Research Center monitor the cerebral blood flow of a patient who has inhaled radioactive xenon gas. Data obtained from this study will help scientists develop better methods for managing stroke patients. From left, Robert Slater, M.D., Edward Cooper, M.D., Martin Reivich, M.D., chief of the Department of Neurology at Philadelphia General Hospital, and Herbert Goldberg, M.D. (NIH Photo #ST-10)

MAYO FOUNDATION STROKE RESEARCH CENTER

The ability of investigators at the Mayo Foundation Cerebrovascular Research Center, under the direction of Clark H. Millikan, M.D., to successfully document the incidence and prevalence of stroke among 55,000 residents of Rochester, Minnesota, represents an important contribution to the understanding of stroke. A study led by Dr. Jack Whisnant, associate director, Program Project on the Natural History of Stroke, showed a significant decrease in the incidence of stroke over the past 15 years in Rochester. This decrease was greater for women than men. While the investigators have not yet been able to pinpoint the cause for this decrease, they have observed that it corresponds with increasingly effective treatment of hypertension in Rochester since the mid 1950's. Efforts are now underway at Mayo to document this apparent beneficial influence of improved management of hypertension on stroke occurrence.

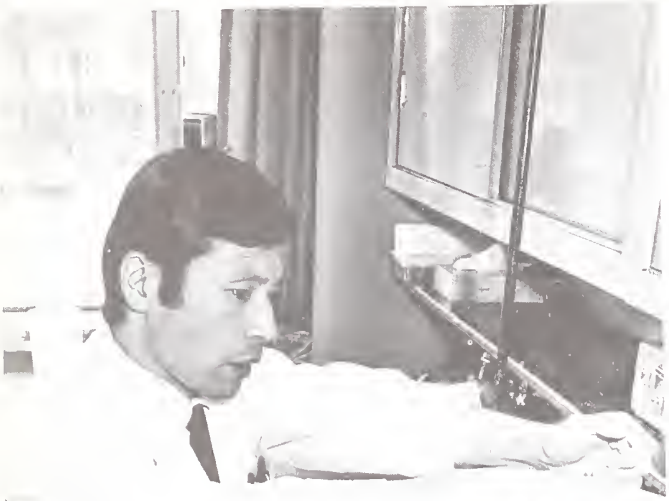
An important area of research conducted at the cerebrovascular center deals with the nature and treatment of transient ischemic attack (TIA). These stroke-like attacks occur without any warning as a result of temporary or partial blockage of the carotid arteries serving the brain. When these attacks occur, the patient suddenly and painlessly loses the function of a portion of his nervous system. Disturbing as the attacks are, function is recovered completely within 12 to 24 hours after onset.

Since approximately one-third of patients suffering from TIA will eventually suffer a stroke, all patients with TIA must be considered as probable candidates for stroke. Procedures for identifying and removing the triggering mechanisms include anticoagulant therapy or, in some cases, surgery.

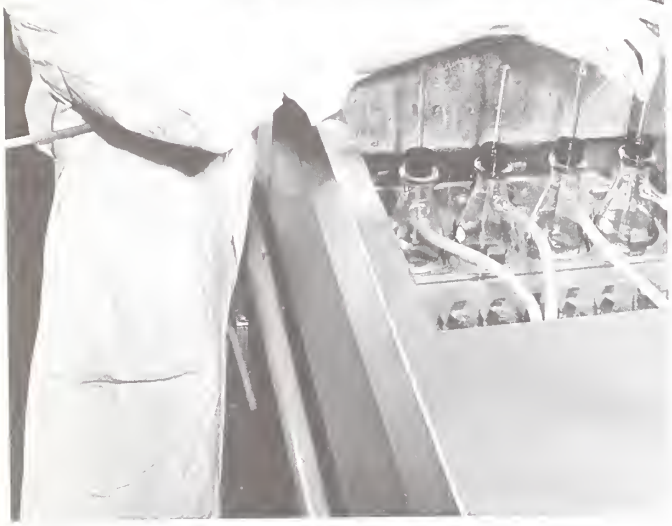
Surgical techniques developed by Mayo researchers to clear blocked portions of the arteries have greatly reduced the dangers inherent in this procedure.

Additional studies on TIA at Mayo have shown that patients treated with anticoagulants following TIA experience significantly fewer strokes than untreated patients. The finding that anticoagulants exert a great influence during the month following the attack will have an important bearing on the future management of TIA. Delay of therapy may prove fatal since the majority of deaths from TIA occur during the month following the attack.

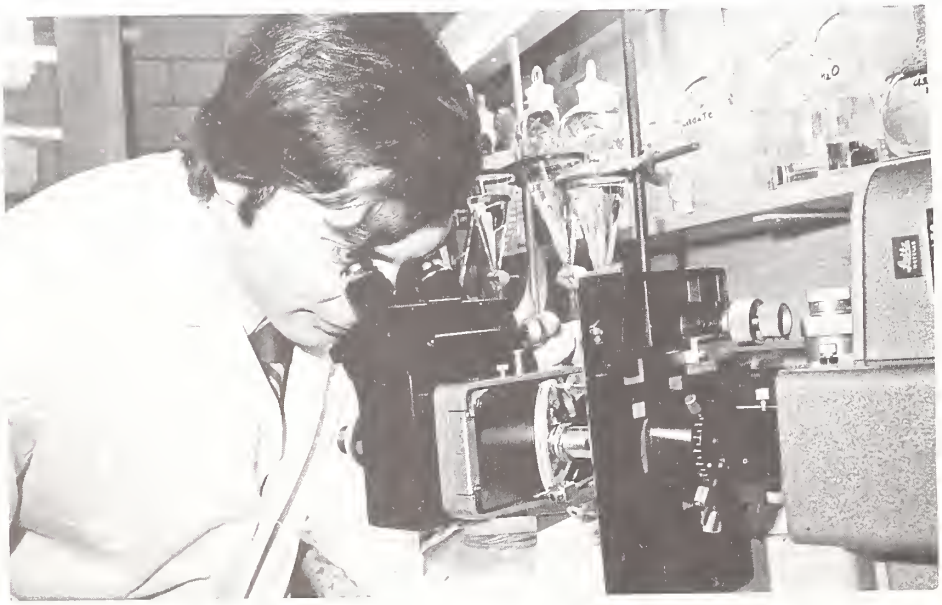
ROCHESTER, MN--Clark H. Millikan, M.D., head of the Cerebrovascular Research Center at the Mayo Clinic, is senior consultant in the Department of Neurology. (NIH Photo #ST-11)

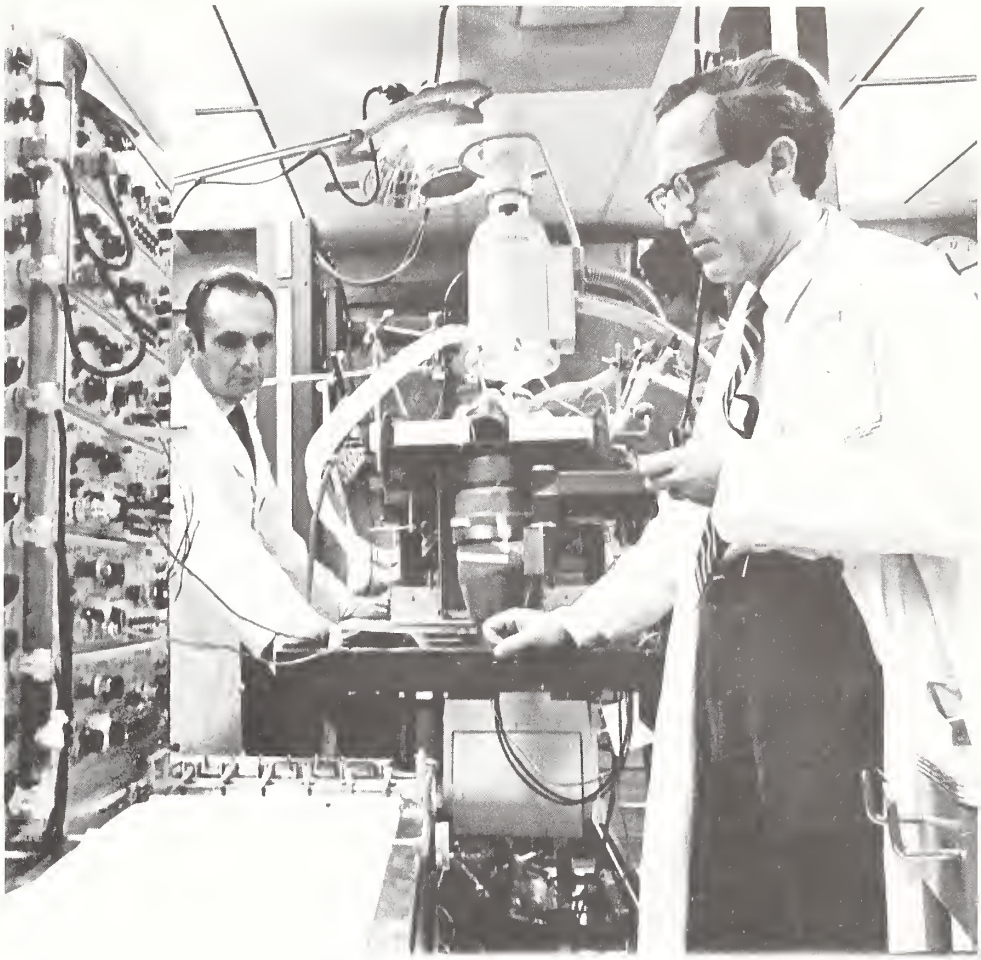


ROCHESTER, MN--Takehiko Yanagihara, M.D., (left) a researcher at the Mayo Foundation Cerebrovascular Research Center, readies the apparatus he designed for studying the effects of reduced oxygen levels on the metabolism of a rabbit's brain. Research in brain metabolism will identify the critical biochemical changes which signal irreversible damage and the mechanisms through which imminent brain damage may be reversed. Dr. Yanagihara's work is supported through the National Institute of Neurological Diseases and Stroke. (NIH Photo #ST-12)

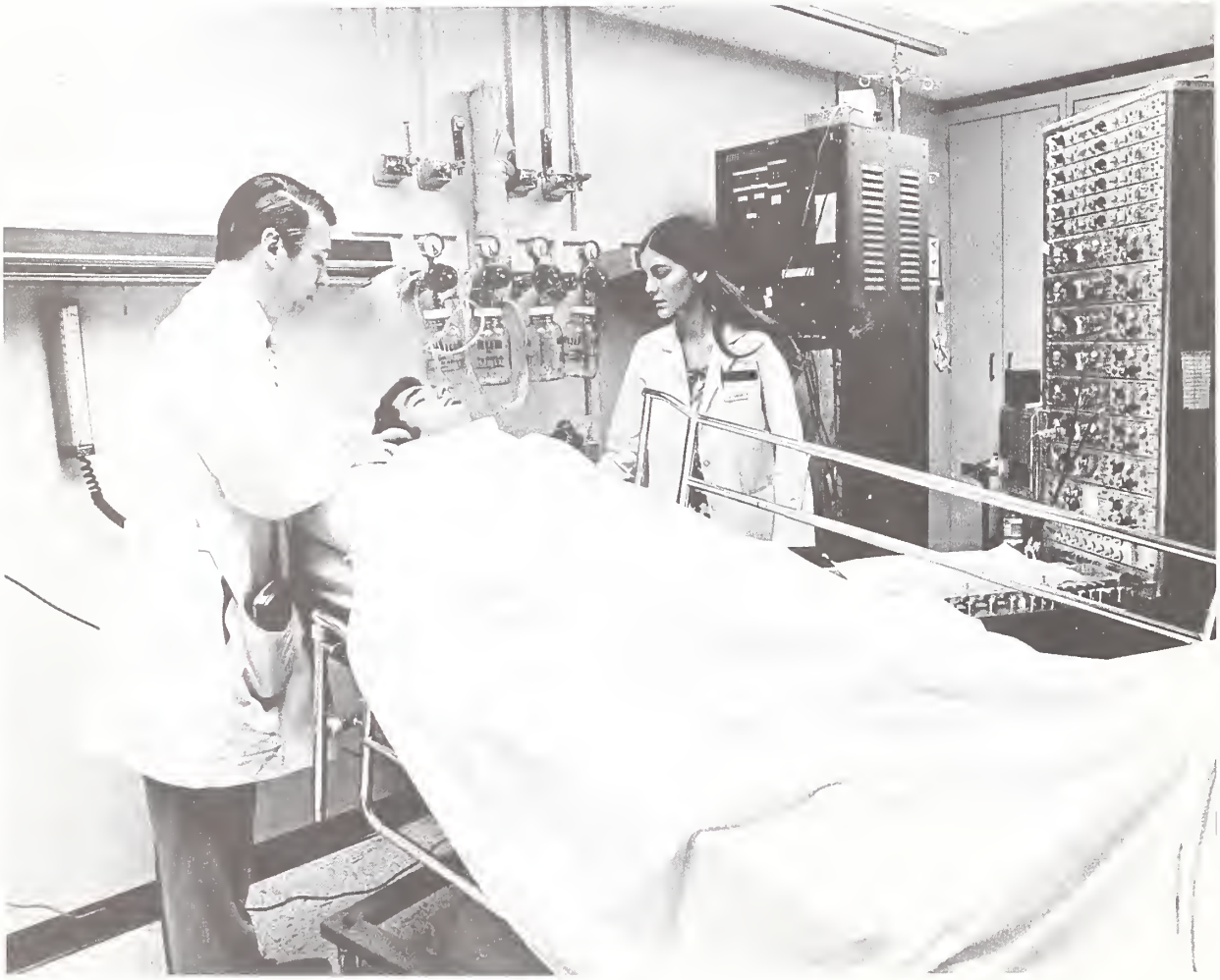


ROCHESTER, MN--Eric Grabowski, M.D., (below) a researcher at the Mayo Foundation Cerebrovascular Research Center, peers through a unique flow chamber he designed to study the surface of cells in circulation. The device, which allows for the control of several factors involved in blood coagulation, is expected to yield valuable information concerning the dynamics of clot formation, a major cause of stroke. His work is supported by the National Institute of Neurological Diseases and Stroke. (NIH Photo #ST-13)





ST. LOUIS, MO--Closely integrated studies of cerebral circulation, cerebral blood volume, and metabolism of glucose in the brain are underway at the Washington University School of Medicine. William M. Landau, M.D. (right), chief of the Department of Neurology, and Michael Ter-Pogossian, Ph.D., study the cerebral circulation of a rhesus monkey using a scintillation probe, a tool that records radioactive isotopes passing through the brain. Scientists at the medical school also are investigating blood coagulation and its relationship to the clinical course of stroke. The National Institute of Neurological Diseases and Stroke supports the Stroke Research Program at the Washington University School of Medicine. (NIH Photo #ST-14)



WINSTON-SALEM, NC--James F. Toole, M.D., head of the Stroke Research Center at Bowman Gray School of Medicine, and Irene Lauver, an acting intern from the University of Florida College of Medicine, examine a model patient in a stroke intensive care unit. With the patient on the tilt table, Dr. Toole and Ms. Lauver are able to monitor his blood pressure, respiration, and brain activity. Patients who are victims of transient ischemic attacks, or little strokes, are candidates for a major stroke. By monitoring the patient's vital functions, the physician can determine whether the danger of stroke is increasing. By adjusting the tilt table he is able to maintain the patient's blood pressure at a stable, low level. Such treatment not only benefits the patient by decreasing the risk of stroke, but also aids the researcher in a better understanding of the relationship between blood pressure and stroke. This research at the Bowman Gray School of Medicine is supported by the National Institute of Neurological Diseases and Stroke, (NIH Photo #ST-15)

WINSTON-SALEM, NC--A patient at the Stroke Research Center at the Bowman Gray School of Medicine is shown wearing a tape recorder that takes continuous readings of his heart's activities over a 24-hour period. The recorder, a Holter monitor, makes continuous electrocardiographic recordings of patients who experience transient ischemic attacks (little strokes). Patients can wear the device while in their home environment during normal activities. Information gained from the recordings will permit researchers at Bowman Gray to learn more about the relationship between heart disease and transient ischemic attacks. The Center is supported by the National Institute of Neurological Diseases and Stroke. (NIH Photo #ST-16)

Do Not
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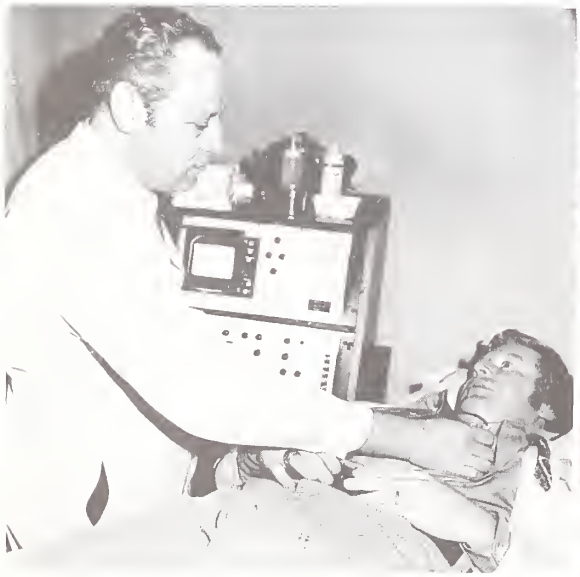
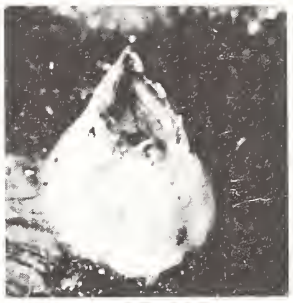


NEWS&FEATURES FROM NIH

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE ▪ Public Health Service ▪ National Institutes of Health ▪ Office of Information ▪ Bethesda, Maryland 20014

October 25, 1973



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NEWS & FEATURES From NIH October 25, 1973

Research Advances

NCI SCIENTIST DEVELOPS PRIMATE MODELS FOR HUMAN CANCER

Studies in monkeys are providing new approaches for diagnosis and treatment of a variety of human cancers in studies at the National Cancer Institute (NCI).

Richard H. Adamson, Ph.D., of the NCI Laboratory of Chemical Pharmacology, has developed three different non-human primate models for human cancers, including the first primate animal model for human acute myelocytic leukemia. (This is an often rapidly lethal form of leukemia that occurs primarily in adults.) Dr. Adamson presented results of his studies on September 21, 1973, at the Sixth International Symposium on Comparative Leukemia Research in Nagoya/Ise-Shima, Japan. The Symposium was sponsored by NCI, the Leukemia Society of America, Inc., and the Japanese Association for the Promotion of Science.

Dr. Adamson reported that macaque monkeys developed acute myelocytic leukemia, lymphoma, and a cancer of connective tissue (hemangiosarcoma) when given high doses of the drug procarbazine over long periods of time. Acute myelocytic leukemia appeared in about five percent of monkeys treated with procarbazine for two to five years.

Four other species of monkeys (the owl monkey, cinnamon ringtail monkey, white-lipped marmoset, and cotton-top marmoset) develop lymphomas and acute and chronic lymphocytic leukemias similar to their human counterparts when inoculated with a virus known as *Herpesvirus saimiri* (HVS). In a series of experiments, leukemia in the owl monkey mimicked the acute lymphocytic

(more)

leukemia of children, including response to treatment with drugs. Cytosine arabinoside or a combination of vincristine and prednisone, for example, caused symptoms of leukemia in the owl monkey to disappear. In owl monkeys with lymphoma, cyclophosphamide produced a disappearance of symptoms.

Because HVS is clearly a cause of cancer in these monkeys, Dr. Adamson is using them as a model for cancer treatment directed specifically toward viruses. He is evaluating the effect of human interferon, a naturally occurring substance which may protect against viral infection. Human interferon is not active in animals other than primates. In preliminary experiments he has found that cytosine arabinoside and adenosine arabinoside prevent the growth of HVS.

Macaque monkeys served as a third model for human cancer. Dr. Adamson produced cancer of the liver in macaques exposed to one of several hazardous agents, including the mold aflatoxin B, the plant product cycasin, and three chemicals of the nitrosamine class (diethylnitrosamine, dipropylnitrosamine, and 1-nitrosopiperidine). In studying liver cancer induced by diethylnitrosamine, the NCI scientist found that this cancer in monkeys resembles the human disease in its resistance to many types of drug treatment. The cancer in monkeys responded, however, to treatment with the drugs methotrexate and adriamycin, or gallium. Methotrexate has been used to treat human liver cancer in clinical studies, but this is the first indication that adriamycin and gallium might merit evaluation against this cancer, Dr. Adamson said.

(more)

Cancer (Cont'd)

He also found that alpha-fetoprotein, a "marker" for human liver cancer, occurs at high levels in the blood of monkeys with the disease. The monkey model also follows the human pattern in that the amount of alpha-fetoprotein in the blood drops as the liver cancer responds to drug treatment or surgery. Liver cancer in macaques may thus provide a valuable new avenue for studying alpha-fetoprotein in the detection of liver cancer and in monitoring the course of treatment.

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NEWS & FEATURES From NIH October 25, 1973

Research Advances

Additional Evidence...

VIRUSES IN HUMAN MILK IMPLICATED IN BREAST CANCER

Additional evidence indicates that viruses present in human milk may play a role in causation of breast cancer.

Jeffrey Schlom, Ph.D., of the National Cancer Institute (NCI) recently described experiment, done in collaboration with Sol Spiegelman, Ph.D., of Columbia University, which revealed that particles found in human milk have components similar to those of viruses known to cause breast cancer in mice. The investigators found that both the human particles and the mouse viruses possessed an inner core consisting of RNA and protein, and a removable outer coat.

Dr. Schlom presented his findings at the Sixth International Symposium on Comparative Leukemia Research held in Japan, September 20, 1973. The symposium was sponsored by NCI, the Leukemia Society of America, Inc., and the Japanese Association for the Promotion of Science.

Having isolated and purified the core material, the scientists plan using it to develop an immunological test for the presence of the virus. Such a test can detect subunits of the mouse virus core in the blood of mice with breast cancer. The scientists will examine the blood of human breast cancer patients for similar traces of the human particle.

"If our theories are correct, Dr. Schlom explained, this may lead to a sensitive diagnostic test for breast cancer in early stages. First, however, we would have to test blood specimens from large numbers of breast cancer

(more)

patients and suitable controls to determine whether traces of the virus consistently appear in women with the disease."

The discovery of virus-like particles in human milk by means of the electron microscopes was first reported several years ago. Subsequent studies by Drs. Schlom, Spiegelman, and others revealed that the particles contain RNA and an enzyme called "reverse transcriptase" which is characteristic of many animal cancer viruses.

In the experiments described by Dr. Schlom, the human virus particles were treated with phospholipase C, an enzyme capable of breaking down the lipoprotein coat of the viruses. They were then subjected to ultracentrifugation, a technique of separating materials according to their density. The core material from human particles was found to have a density of 1.26-1.27 grams per milliliter, the same as that from the mouse virus core. Since this density was higher than that of intact viruses (1.16-1.19), or normal constituents of the milk, the method yielded purified samples of core material.

These experiments provide further evidence that the human virus particles may be cancer viruses. In addition, the isolation and purification of the core material makes possible further tests to determine the relationship of the particles to known cancer viruses and to specific human cancers.

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Research Advances

IN THE LITERATURE:
Proceedings of the Society for Experimental Biology and Medicine, May 1973

SENSITIVE NEW TEST DETECTS MYCOPLASMA INFECTIONS

Scientists at the National Institute of Allergy and Infectious Diseases (NIAID) have developed a sensitive new test for detection of antibody to *Mycoplasma pneumoniae*, an organism that causes outbreaks of acute respiratory infections during late summer and early fall. The test, a modification of a radioimmunoprecipitation procedure, should enable scientists to learn more about the disease pattern of this organism in man.

The test was developed by Robert M. Chanock, M.D., chief of NIAID's Laboratory of Infectious Diseases, and Dr. Helmut Brunner, a visiting scientist from the Institute for Medical Microbiology, West Germany. A description of the test appeared in the May, 1973 issue of the *Proceedings of the Society for Experimental Biology and Medicine*.

Scientists and physicians have become increasingly concerned about the mycoplasmas. These organisms share certain characteristics with bacteria and viruses in the disease symptoms they produce, yet are dissimilar in the way they produce the diseases. Evidence has been accumulating that implicates *Mycoplasma pneumoniae* as the cause of an acute respiratory disease that mainly affects people between the ages of five and 25. One recent study revealed that *M. pneumoniae* is the primary cause of pneumonia in school age children.

The new radioimmunoprecipitation (RIP) test involves incubating small amounts of radioactively labeled mycoplasma antigen--lipoprotein from the

(more)

Mycoplasma Infections (Cont'd)

M. pneumoniae cell membrane--with serum being tested for antibody. Anti-human gamma globulin or antihuman whole serum, prepared in animals, is then added to precipitate the antigen-antibody complex. After overnight incubation, the material is centrifuged. The amount of radioactivity deposited in the precipitate is measured to indicate the amount of antigen which has been bound to specific antibody, and thus, the presence or lack of antibody in the serum sample.

Using RIP in this way, Drs. Chanock and Brunner studied sera from 10 volunteers infected with the *M. pneumoniae* strain via the nasopharynx. The RIP test was considerably more sensitive in detecting antibody than conventional tests such as complement fixation and immunofluorescence.

The new test provides a useful tool in studying the disease patterns of *M. pneumoniae*, since RIP can measure antibodies of the immunoglobulin A class (IgA). These are the predominant functional immunoglobulins in local secretions that provide protection against respiratory infection. Previous attempts to demonstrate antibody to *M. pneumoniae* in nasal or bronchial secretions of persons infected with organisms have either failed or yielded conflicting results. However, using RIP, Dr. Chanock found that a high proportion of volunteers inoculated intranasally with *M. pneumoniae* developed a fourfold or greater rise in IgA antibody in nasal secretions. The role of local antibody to *M. pneumoniae* in the disease caused by this organism is currently under investigation and may have significance in mycoplasma vaccine development.

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Photo Feature

WOMEN AT NIH AID RESEARCH

Elizabeth W. Chu, M.D., head of the Cytopathology Section of the Laboratory of Pathology, National Cancer Institute, conducts diagnostic studies of cells from Clinical Center patients. Her research is also concerned with the influence of drugs and hormones on the development of cancer in hamsters and mice. Dr. Chu is currently investigating the long-term effects of birth control pills fed to mice and of alcohol in the drinking water of hamsters. (NIH Photo #1139)

(more)

Women (Cont'd)

Research biologist Suzanne Amsbaugh (left) examines a rat for caries as part of the National Caries Program of the National Institute of Dental Research. Ms. Amsbaugh conducts many of the Institute's rat and hamster research experiments. One such project involves 72 rats which receive caries-producing enzymes in their diets for eight weeks. The fissures in the rat teeth are then observed and the results recorded and compared with previous research findings. (NIH Photo #1140) Judy Mahaffey (right), a computer systems analyst with the Division of Computer Research and Technology, meets with scientists to design computer systems which standardize the extensive data from their research projects. She develops flow diagrams of the systems for data collection and codes the participating responses. (NIH Photo #1141)

(more)

Women (Cont'd)

Trudy Kenny (above right), a Division of Computer Research and Technology (DCRT) computer programmer, works with computer users through the Programmer Assistance and Liaison Unit (PAL). When systems problems occur, Ms. Kenny studies and diagnoses the difficulty and then guides the user in rewriting and recoding. Ms. Kenny and other programmers in the PAL Unit compile the solutions to frequent problems (inaccurate coding being the most common) and distribute a current technical publication (Interface). (NIH Photo #1142) Josephine Campbell (below), a DCRT computer aide, checks the read-out on a WYLBUR terminal which indicates the location of approximately 22,440 computer tapes in the computer library. Handling about 100 new tapes a day, Ms. Campbell maintains an accurate daily tape log and assigns the tapes to computer operators. (NIH Photo #1143)

#

NEWS & FEATURES From NIH October 25, 1973

News Feature

NIH EXPLORES MANY DIGESTIVE DISEASES

Because digestive diseases affect so many American families, the National Institutes of Health is giving considerable attention to research in this area. Digestive diseases include such well-known disorders as peptic ulcer, regional ileitis, and ulcerative colitis, and encompass many other diseases of the intestinal tract and associated organs about which too little is known. These include cirrhosis of the liver, gallbladder disease, pancreatitis, and intestinal malabsorption.

Digestive diseases are among the most common illnesses in this country, ranking second only to diseases of the heart and circulation in the number of physician office visits or house calls. Cirrhosis of the liver, for example, is the fifth most common cause of death in male adults in America.

Peptic ulcer or its symptoms will strike about 10 percent of all adults in the United States at some time in their lives. Many victims of ulcerative colitis are afflicted for years with their disorder and must undergo extensive and repeated surgery. Diseases of the stomach and intestines may afflict persons of any age, but most often affect those in the younger and middle-aged groups at the peak of their most vigorous and productive periods, often causing prolonged and expensive hospitalization and countless social and emotional problems.

The economic and social cost of digestive diseases is also significant. The loss due to disability, and the income loss due to premature death, is calculated at $11 billion annually. Of all disease categories, digestive diseases rank third in causing economic loss, exceeded only by cardiovascular

(more)

disease and accidents. The annual economic loss to the United States due to peptic ulcer alone is calculated at just under $1 billion.

The National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) bears responsibility for the Federal Government's program of research in the field of digestive diseases. Through numerous grants to scientists at research centers across the country, many ailments of the digestive tract are being studied. Research progress has been achieved through the most intensive and comprehensive laboratory experiments and clinical trials.

In 1972, NIAMDD began investigations of gallbladder disease at the Indian Health Service's Phoenix Indian Medical Center. Phoenix is field headquarters for NIAMDD epidemiological and clinical studies of gastrointestinal diseases, arthritis, and diabetes among populations of American Indians. Arizona's Pima Indians, in particular, are a unique population in which there is an unusually high prevalence of diabetes (10-15 times the U.S. norm) and an even higher incidence among women of gallbladder disease. This makes them an excellent group for biomedical research focused on these diseases.

An outstanding example of the application of fundamental research information to solution of problems of disease is that of an NIAMDD grantee at the Mayo Clinic who has shown that long-term oral administration of a bile acid, chenodeoxycholic acid, can result in dissolution of long-standing cholesterol gallstones. This is the first report of gallstone dissolution in man under controlled conditions using a single agent on a rational basis. Preliminary findings were sufficiently promising that the Institute has now initiated a cooperative clinical trial of this therapy to test nearly 1,000 patients over a five year period.

(more)

Digestive Diseases (Cont'd)

As part of the Institute's plan to intensify program efforts, the National Cooperative Crohn's Disease Study has been initiated. This study is designed to determine the efficacy of several commonly used regimens in the treatment of Crohn's disease, a chronic inflammatory disease of the bowel also known as regional ileitis, which causes prolonged periods of hospitalization and frequently leads to surgical removal of portions of the intestine. The study, initially involving eight university medical centers, will be a controlled, randomized clinical evaluation of three currently used drugs to determine their effectiveness.

#

NEWS & FEATURES From NIH

October 25, 1973

Photo Feature

MARINE INVERTEBRATES OFFER UNIQUE RESEARCH ADVANTAGES

Only skin and protective membrane cover the octopus brain, making surgical manipulation comparatively simple. (NIH Photo #1144)

Marine invertebrates, such as barnacles and starfish, are becoming increasingly valuable to the biomedical research community due to the unique advantages they offer scientists.

Researchers in the Animal Resources Branch of the Division of Research Resources (DRR), which develops animal models for studies related to human health, have found that many invertebrate animal organisms offer simple anatomical and physiological systems and can be investigated with ease.

According to DRR's Program Analysis Branch, some 263 NIH-supported studies are now using marine invertebrates.

Arthropods--such as crabs, lobsters, and barnacles--are the most frequently studied of the marine invertebrates. There are also several studies of organisms in the mollusk category--oysters, clams, squid, and snails. A smaller number of projects use the echinoderms--starfish, sea urchins, and sea cucumbers.

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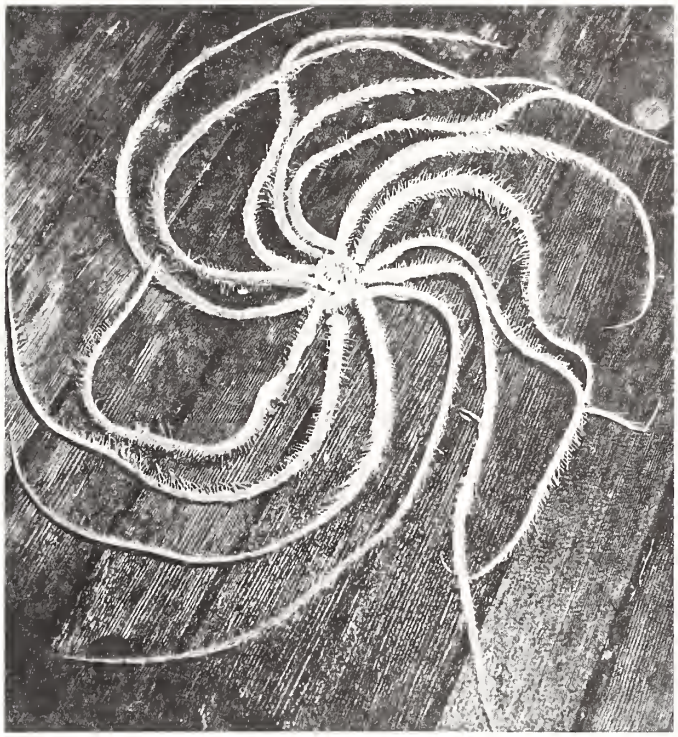
Invertebrates (Cont'd)



Marine researchers have found that a starfish can reproduce itself from only a small part of its central disc or from a piece of its arm only 2/5 of an inch long. When cut in half, each part will grow into two animals in about three months. (NIH Photo #1145)

Dental researchers are attempting to unravel the mystery of "barnacle glue," the excretion which allows the barnacle to adhere to boat hulls, pilings, and other objects in the water, for possible use as a cement for dental fillings. Another barnacle is shown on the cover page of this issue. (NIH Photo #1146)

#

News Feature

NEW NIH CONTRACT GUIDE GIVEN WIDE DISTRIBUTION

The National Institutes of Health has issued its latest policy statement concerning the selection and use of the contract mechanism for the support of biomedical research.

The current issue of the publication, the *NIH Guide for Grants and Contracts*, will be given the widest distribution in the biomedical research and engineering development communities, in an effort to reach those individuals who have not seen previous issues of the *Guide* and may be unaware of NIH contract-supported activities.

Basically, contracts are used for support of research and development in the light of one or more of the following considerations:

- The awarding Institute or Division has identified a need for certain research work, has determined that the work must be done outside its own facilities, and has taken the initiative for undertaking the activity;
- The objective is the acquisition of a specified service or end product;
- The collaboration of a number of institutions must be obtained, and work must be coordinated so that the data collected can be combined for statistical analysis; or
- The NIH awarding unit participates in the direction and control over the manner of performance or timing of the work.

The *Guide* contains revised descriptions of research programs of those NIH Institutes and Divisions which use contracts as the method of support of

(more)

research or for provision of research services. It provides a specific addressee from whom additional information may be obtained.

In addition, a handy tear sheet is available in the back of the *Guide* for the use of those interested in being included on appropriate mailing lists. It is suggested that those making such requests be selective--for example, deans, vice-presidents for research, and administrative personnel responsible for sponsored research should request both the regular *Guide* and all supplemental issues. Individual investigators should normally limit their choices to selected programs within their own primary field of research.

Copies of the publication, *NIH Guide for Grants and Contracts, Vol. 2, No. 7,* may be obtained from the Grant and Contract Guide Distribution Center, NIH, Division of Research Grants, Westwood Building, Room 206, Bethesda, MD 20014.

#

Medical News Tip

EFFECTS OF CHEMICALS ON REPRODUCTION--Scientists at the National Institute of Environmental Health Sciences (NIEHS) are using test-tube cultures of fertilized ova (eggs) from mice, rats, and rabbits to study the effects of added chemicals on reproduction and gestation, as well as the role of the mother in birth defects caused by environmental influences.

The researchers also use whole fertilized eggs. They first expose an egg to a chemical, then re-implant it into the uterus. After birth, normalcy or defects can be established.

These living-animal and test-tube systems are being validated with well-studied chemicals such as thalidomide.

These studies provide a new approach to determining why many unexplained birth defects in animals and man come from environmental pressures on the mother.

For additional information about NIEHS studies on effects of chemicals on reproduction, contact: NIEHS Information Office, Post Office Box 12233, Research Triangle Park, NC 27709, phone (919) 549-3345.

#

Capsules

Factual Fillers

PARKINSON'S DISEASE--Parkinson's disease is one of the severely crippling chronic disorders of the nervous system, according to the National Institutes of Health. It most frequently attacks people in their 50's and 60's, and is thought to be increasingly prevalent as the average life-span increases.

BRAIN SCANNING--Radioisotopic brain scanning is rapidly becoming one of the essential methods of cerebrovascular diagnosis, according to the National Institutes of Health. It entails injection or inhalation of radioisotopes instead of dye, and production of pictures by radiation detectors.

MULTIPLE SCLEROSIS--Multiple sclerosis is the most common demyelinating (loss of fatty sheath surrounding nerve fiber) disease of man, according to the National Institutes of Health. It affects primarily young adults in temperate climates, such as those of North America and Europe. In the United States alone, an estimated 250,000 patients suffer from the disease. Many thousands of others suffer from closely related sclerosing disorders.

EPILEPSY--Epilepsy is a term used to describe both a set of symptoms and the underlying mechanism that causes them. Precisely defined, epilepsy is "recurring, abnormal, uncontrolled electrical discharges of brain cells." The symptoms of epilepsy are called seizures because people used to think that a victim had been "seized" by an evil spirit, according to the National Institutes of Health.

Factual Fillers (Cont'd)

FETAL GROWTH RATE--The rate of growth of the human fetus varies remarkably. Parental stature, socioeconomic factors, parity (number of previous births to mother), maternal nutrition and smoking (or tobacco chewing), and geographic situation may all contribute to this great variation in mean birth weight, according to the National Institutes of Health.

COMMUNICATION PROBLEMS--All ages are affected by problems of communication. They are particularly noticeable in the very young and the aging. It is especially important that the problems be diagnosed early in children since language is largely developed before a child begins school, according to the National Institutes of Health.

POOR SPEECH--Approximately 500 out of every 10,000 Americans have a speech disorder, according to the National Institutes of Health.

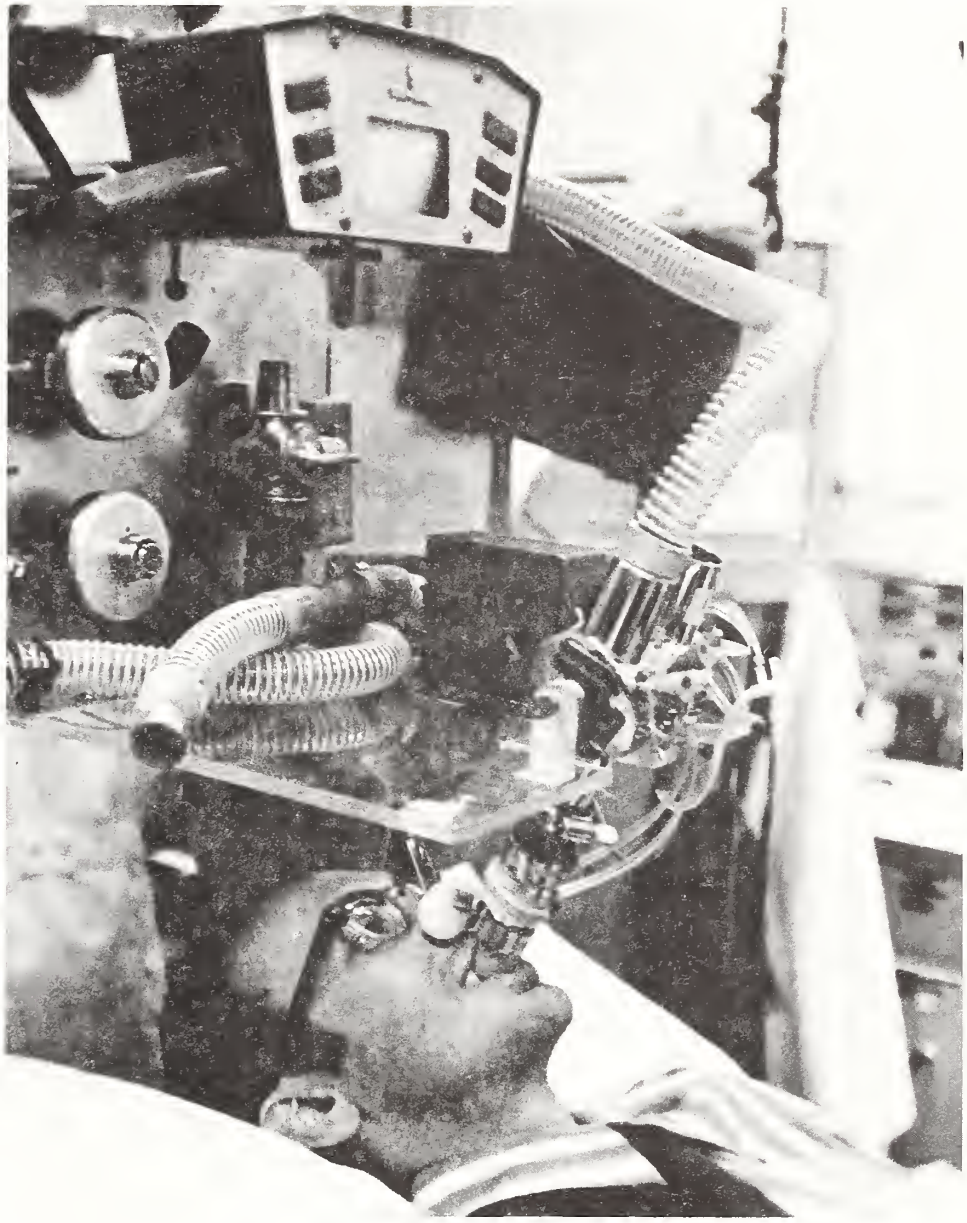
SPEECH TROUBLE--The larynx is the passageway for air which contains the vocal cords--folds of tissue that govern speech. Computer diagnosis of laryngeal disease has become an invaluable aid to the clinician, according to the National Institutes of Health.

SPINA BIFIDA--As the unborn child develops, the vertebrae in the backbone grow around the spinal cord to protect and support it. In spina bifida, one or more of these vertebrae fail to close, leaving an incompletely closed cylinder and an exposed portion of the spinal cord, explains the National Institutes of Health.

(more)

Capsules (Cont'd)

Research Illustrated



This young man who is partially paralyzed by polio is participating in a pulmonary function test funded by the National Heart and Lung Institute. Special respiratory equipment controls the flow of gasses that he inhales. With such tests, scientists can measure the volume and flow rates of his respiration. The patient can see certain results through the clear lucite shelf provided for him. (NIH Photo #1147)

#

New Publication:
Pneumococcal Infection

A new publication, *Pneumococcal Infection*, has been released by the National Institute of Allergy and Infectious Diseases (NIAID).

Pneumococcal pneumonia is just as common today as it was before the advent of "wonder drugs." Each year in the United States there are between 200,000 and 400,000 cases of pneumococcal pneumonia, with as many as 45,000 deaths.

A tiny organism, *Diplococcus pneumoniae*, is the cause of pneumococcal pneumonia. Commonly called pneumococcus, it is one of the major bacterial agents of man and is responsible for a wide variety of infections. Pneumococci account for nearly 80 percent of all acute *bacterial* pneumonias.

Otitis media (inflammation of the middle ear)--a serious illness of early childhood--is also caused by pneumococci. Left untreated, the disease may result in deafness.

D. pneumoniae is found throughout the world as a normal inhabitant of the human upper respiratory tract. An estimated 30 to 70 percent of healthy persons harbor pneumococci at any one time. These healthy carriers play a larger role in spreading the organisms than do patients who are ill with pneumococcal illnesses.

Science writers can obtain a free copy of this publication from:

NIAID Information Office
Building 31, Room 7A-32
Bethesda, MD 20014
Phone (301) 496-5717

#

News Releases Issued

Summaries of NIH releases sent out since the last issue. For a copy of any of these, please write or call.)

SICKLE CELL DISEASE--The National Heart and Lung Institute (NHLI) has established five new Comprehensive Sickle Cell Disease Centers and continued support of 10 similar Centers that were started in 1972. The new Centers are at the University of Chicago, Children's Hospital Medical Center of Cincinnati, the University of Miami, Wayne State University, and Martin Luther King, Jr. General Hospital of Los Angeles. Also funded were 11 new Screening and Education Clinics bringing the clinics total to 26, as well as four new targeted research projects raising the projects total to 28.

BLOOD DISEASES--The National Heart and Lung Institute has announced its intention to establish a limited number of National Research and Demonstration Centers for heart and blood-vessel diseases, lung diseases, blood diseases, and blood resources. By demonstrating new and improved preventive, diagnostic, and therapeutic measures in a community setting, the Centers should hasten the widespread application of new knowledge. The Centers will likely be part of or closely affiliated with major medical complexes.

PROTECTING HUMAN SUBJECTS--HEW Secretary Caspar W. Weinberger has announced regulations to provide additional protection of human subjects involved in HEW-supported research and development activities. The proposed regulations would amplify the existing requirements that grantee and contractor organizations establish initial and continuing review mechanisms to govern all HEW-

(more)

News Releases Issued (Cont'd)

funded activities in which human subjects are placed at risk. This action is the first of several steps leading to the development of a uniform Federal policy. The *Federal Register* published the proposed regulations on October 9, 1973.

#

Editors of publications may request glossy prints of numbered photographs that appear in the regular issue.

NEWS & FEATURES From NIH
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Building 31, Room 2B-10
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November 10, 1973

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NEWS & FEATURES From NIH November 10, 1973

Research Advances

FOOD PRESERVATIVES AFFECT HUMAN CELLS

A recent study funded by a National Institute of Neurological Diseases and Stroke (NINDS) contract indicates that food additives may be hazardous to your health.

Results show that fatty acids and other chemical compounds commonly used to inhibit the growth of food-spoiling bacteria have an impact on mammalian cells as well.

A team of scientists from Georgetown University and NINDS conducted laboratory tests which exposed human liver and intestinal cells and chicken embryo cells to varying concentrations of the chemical compounds used to preserve beverages, and canned and frozen foods. In every case, additives inhibited cell growth. At high concentrations, mammalian cells were killed and their shapes altered. Under microscopic examination, the human cells appeared to be unusually opaque and to have ragged outlines.

T. Sreevalsan, Ph.D., associate professor of Microbiology at Georgetown University, pointed out that the investigation involved only tissue cultures, and that different results might have been obtained if whole tissues or animals were used. "There may be a mechanism whereby the stomach tissue in a whole organism is able to detoxify the compounds in humans." However, Dr. Sreevalsan noted that while more research is planned for the future, "present evidence would urge caution in eating large quantities of food containing such additives." Similar considerations would apply to such commonly-used drugs as aspirin, a fatty acid compound.

(more)

Preservatives (Cont'd)

Coinvestigators with Dr. Sreevalsan were Elliott Ginsburg and Daniela Salomon, research assistants, Department of Microbiology, Georgetown University School of Medicine and Dentistry; and Ernst Freese, Ph.D. Laboratory of Molecular Biology, NINDS.

This research was published in the August 1973 *Proceedings of the National Academy of Sciences*.

#

PRIMATE RESEARCH--Non-human primates such as apes and monkeys are man's closest relatives in the animal kingdom, and are therefore valuable in medical research projects, according to the National Institutes of Health.

MINORITY SCHOOLS--The National Institutes of Health is working to upgrade the biomedical research capabilities in institutions of higher learning which have predominantly ethnic minority student bodies.

SUDDEN DEAFNESS--Research indicates that sudden deafness might be related to systemic diseases including fat embolism and hypercoagulation (diseases that block the circulation), according to the National Institutes of Health.

Research Advances

SALIVARY SECRETIONS AFFECT TASTE IN RATS

Salivary secretions affect all four taste factors in rats. This finding results from a study of a wide range of concentrations of the principal elements of taste (sweet, sour, salty, and bitter) which was supported by the National Institute of Dental Research (NIDR).

NIDR grantees at Harvard University found that removal of the submandibular and sublingual glands in rats caused almost as many changes in taste preferences as removal of all salivary glands. They found little difference between the reactions of rats with all their salivary glands and those without parotid glands.

Understanding the effects of saliva on taste, food consumption, and health is important in a number of human diseases which leave the mouth dry or impair the senses of taste and smell.

Frank A. Catalanotto, D.M.D., and Edward A. Sweeney, D.M.D., note that like people, rats prefer sweets and low concentrations of salt, but dislike strong ones. The animals avoid acid and bitter solutions unless these solutions are very weak.

The investigators say that removing the two sizeable submaxillary glands and the small sublingual glands drastically changes rat taste-preferences. The most striking change is the acceptance of much more concentrated, bitter, quinine solutions. Also, these animals show a sugar preference only for very high concentrations, and consume larger amounts of strong salt solutions. Their tolerance for acidity varies, and does not increase as predictably as that of animals with no salivary glands.

(more)

Salivary Secretions (Cont'd)

There is evidence that animals without saliva cannot discriminate well among low concentrations of several taste elements, but the role of specific groups of salivary glands has not previously been studied statistically for all four taste factors over a wide range of concentrations.

Drs. Catalanotto and Sweeney observe that removing the submaxillary and sublingual glands removes the chief lubricant of the taste buds on the tongue, and may damage their physiological as well as their physical condition. The scientists also note that after a considerable time, taste-limited animals tend to avoid very concentrated bitter and acid solutions that were previously accepted presumably because of metabolic changes due to the quinine and hydrochloric acid rather than to any ability to discriminate by taste. Control of salt intake seems to disappear permanently after loss of taste.

Lack of taste and of fluid for lubrication can reduce an animal's consumption of food. But, even when rats given oil-soaked food to compensate for loss of fluid ate as much as intact animals, those without salivary glands grew more slowly than intact or partially desalivated animals. This finding may indicate that food is not as well digested without salivary enzymes.

These findings were reported in the August 1973 issue of *Archives of Oral Biology*.

#

Research Advances

IN THE LITERATURE:
Journal of Immunology, May 1973

RAGWEED PREPARATION PROVES USEFUL IN IMMUNOTHERAPY OF HAY FEVER--National Institute of Allergy and Infectious Diseases (NIAID) grantees are studying a new ragweed preparation containing a high concentration of the important pollen antigen E in an attempt to improve desensitization shots for hay fever.

The preparation was obtained by polymerization--a chemical process which links together any number of identical molecules. Scientists at Northwestern University and Abbott Laboratories, Chicago, report that polymerized ragweed antigen E is at least as antigenic as antigen E alone and that, judging from its behavior in laboratory and animal studies, it might be expected to produce fewer side effects in persons undergoing hay fever immunotherapy.

The scientists obtained polymers of varying molecular weights by treating ragweed antigen fractions with the chemical glutaraldehyde. These aggregates (or polymers) of the antigen did not seem to have any antigenic determinants (antibody combining sites) not found on a single antigen E molecule. In addition, all determinants found on antigen E were also present on the polymers.

One polymer, designated LMW-P-RW, seemed to be the most antigenic. It remained in the circulation of animals longest and resulted in a more significant immune response.

Much larger doses of polymerized than single antigen E were required for histamine release from blood cells of hay fever sufferers; a large dose of LMW-P-RW was also needed to obtain an allergic skin reaction in one of the investigators who served as a test subject. These findings indicate a

(more)

Ragweed Preparation (Cont'd)

diminished reactivity with the sensitized mast cells which play such an important role in allergy and suggest that large doses of the polymerized preparation might be used in immunotherapy without fear of disabling side effects.

Dr. Roy Patterson and his associates at the NIAID Asthma and Allergic Disease Center at Northwestern University will include polymerized antigen E in their clinical investigations. Dr. Patterson, Irena M. Suszko, and Floyd C. McIntire reported the results of their laboratory and animal studies in the *Journal of Immunology*, May 1973.

#

POPULATION RESEARCH--The National Institutes of Health is studying new and improved methods of contraception, medical effects of contraceptives in current use, and social science aspects of population.

SUDDEN DEATH--The sudden infant death syndrome is a major cause of death in infants who are between one month and one year old. The National Institutes of Health is studying this syndrome that kills three infants out of every thousand live births.

Photo Feature

THOUSANDS OF AMERICANS STUDIED FOR HYPERTENSION

The Hypertension Detection and Follow-Up Program of the National Heart and Lung Institute involves the examination and treatment of thousands of Americans by specially-selected physicians in several health institutions.

Involved in the studies are community-based populations that include women and young individuals in whom no damage to heart or kidney is yet apparent. Measuring a patient's blood pressure is extremely important because a seriously-elevated reading may be the first clue to future trouble. (See photos of Drs. Finnerty, Stamler, and Kass.)

Physicians are evaluating methods of controlling blood pressure in hypertensive individuals. It will require several years before data are available on the reductions in the disabilities or in early deaths these patients might have experienced if their high blood pressure had remained untreated.

(more)

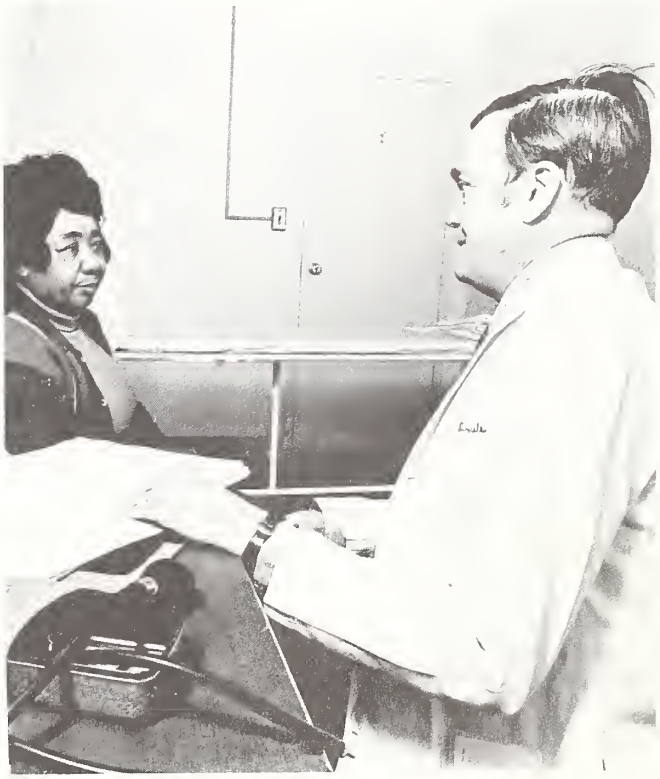
Some physicians in the Hypertension Detection and Follow-Up Program are explaining the program on radio and televisions programs. Here, Morton Maxwell, M.D. (left), of Cedars-Sinai Medical Center, discusses hypertension on the David Susskind program. (NIH Photo #1148)

Hypertension (Cont'd)

At Georgetown University, Frank A. Finnerty, Jr., M.D. (left photo), double-checks a man's blood pressure reading. Harold W. Schnaper, M.D. (far right), and Albert Oberman, M.D., at the University of Alabama are treating hypertensive patients. (NIH Photos #1149, 1150)

(more)

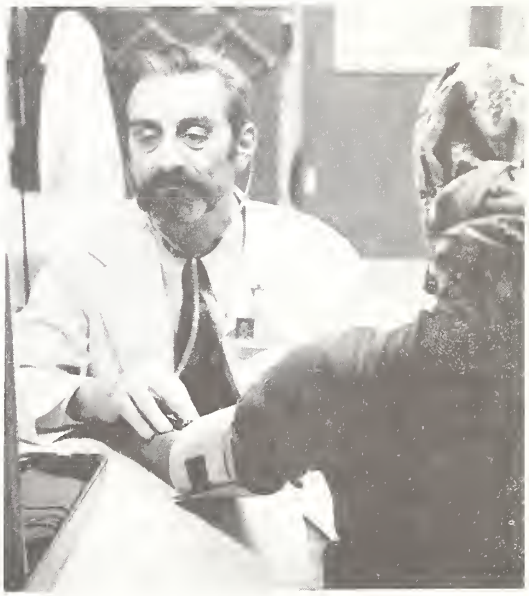
Hypertension (Cont'd)



Among the principal investigators in the Hypertension Detection and Follow-Up Program are Jeremiah Stamler, M.D. (above), of Northwestern University; C. Hilmon Castle, M.D. (upper right), of the University of Utah; and George Entwisle, M.D. (right), of the University of Maryland. (NIH Photos #1151, 1152, 1153)

(more)

Hypertension (Cont'd)



A good example of the community-based aspect of the Hypertension Detection and Follow-Up Program is seen in Claxton, Georgia (above), where some residents report to this former private home in which Health Officer Curtis G. Hames, M.D., is working. Other principal investigators include Herbert Langford, M.D. (left photo), of the University of Mississippi and Edward Kass, M.D. (right photo), of Boston City Hospital. (NIH Photos #1154, 1155, 1156)

#

Photo Feature

RAT-LIKE DEGU FROM CHILE BORN WITH TWO THYMUS GLANDS

The rat-like degu (*Octodon degus*) from Chile possesses an unusual biological quirk--it has two anatomically separate thymus glands.

Immunologists hope to use the degu to decipher the function of the thymus, the tiny master organ which, in early life, sets up the immune defense mechanisms for the body.

The full-grown degu weighs less than 11 ounces. However, this little trumpet-tailed rat from the lower altitudes of the Andes Mountains of South America is a valuable research animal because it is born with two thymus glands. (NIH Photo #1157)

David K. Boraker, Ph.D., an immunologist at the University of Vermont in Burlington, is developing a pedigreed colony of degus (sometimes referred to as a trumpet-tailed rat) for medical experimentation. The colony now numbers over 300. His research is supported by the Division of Research Resources.

(more)

Thymus (Cont'd)

In comparison with the traditional experimental animal, the mouse, the anatomical location of the double thymus in the degu makes it far more accessible for thymic biomedical research, according to the immunologists at the University of Vermont. Also, Dr. Boraker believes, "The thymus in the mouse has pretty well done its job when the animal is born."

The thymus in the human and in most mammals is a single structure located in the upper chest cavity. The thymus is of fundamental importance in the development of the immune system of the body, primarily in establishing the body's defense mechanism in late fetal life and early life after birth--up to about 14 years of age in the human. After this, the organ usually undergoes fatty metamorphosis and atrophy (decreasing in size and wasting away).

The degu is consistently born with a cervical thymus (located in the neck), and a mediastinal thymus (located in the upper cavity). According to the Vermont researchers, the cervical thymus can be removed quite easily without harming the animal.

"One of the great enigmas in immunology is that it is not known for sure how the thymus accomplishes its duty," Dr. Boraker points out. "We know a great deal about it, but there are still some very intriguing mysteries about the thymus. For instance, it is reported that the thymus is a hormone secreter. This is controversial. Perhaps, with continued study of the degu, we can ultimately seek out the precise morphological process of this organ which is considered to be directly responsible for developing the body's immune system."

#

NEWS & FEATURES From NIH November 10, 1973

News Feature

RESEARCH INTO GENETIC DISEASES OFFERS HOPE FOR AFFLICTED

There is no convincing evidence that any genetic disease is actually new or more prevalent today than in past generations. The recent advances in human genetic knowledge have, however, brought sharply into focus the problem's staggering dimensions. Coincidental has been a growing understanding of how we may begin to cope with these diseases in a substantive way.

It is now known that more than a thousand serious diseases and disorders are wholly genetic in origin, resulting in much illness, malformation, and mental retardation.

Taken individually, most of these diseases are rare, occurring in no more than one per 10,000 to 20,000 of the population. But a respectable number are far more common and widespread, bringing the overall incidence closer to one in 200. This translates to an annual birth rate in the United States of approximately 20,000 genetically-deficient babies.

Fortunately, with modern medical care many genetically-handicapped children who would have died in infancy only a few years ago have their life span greatly extended. Still, there is often much to be desired in the quality of their lives, and there has been a corresponding increase in the emotional and economic burdens borne by affected families. The obligation of society to assist in the care of these children and help make their lives as satisfying as may be possible has been increased to a similar degree.

(more)

Genetic Diseases (Cont'd)

Among specific genetic disorders singled out for research by the National Institutes of Health are cystic fibrosis, hemophilia, Down's syndrome (mongolism), muscular dystrophy, Huntington's chorea, Cooley's Anemia, and Tay-Sachs disease.

Each of these disorders is a target for better management and control based on the prevalence and severity in the population and measured in terms of the resultant deaths, suffering, and disability.

The genetics program of the National Institute of General Medical Sciences (NIGMS) has been established as the primary resource to interconnect and fund a wide range of studies applicable to whole categories of heritable disease.

The strategy is to generate new concepts and technologies by which genetic disorders sharing common courses of abnormality and transmission may be precisely defined. It is hoped the search can progress from relatively simple single-gene conditions to the complex multiple-gene and chromosomal disorders whose pathological pathways are at present almost completely unknown.

Because genes direct the manufacture of all body proteins, every gene defect results in some faulty protein--whether an enzyme or a structural protein. Theoretically, at least, each protein is subject to discovery and assay. Successful endeavors of this sort bring immediate diagnostic promises and point the way to rational therapy.

Phenylketonuria (PKU) is a good example. This metabolic disorder results from an inherited enzyme defect in which the amino acid phenylalanine,

(more)

found in many foods, is improperly metabolized, causing severe brain damage in children during their early years of growth. Discovery some years ago of the genetic block made it possible to lessen and prevent the damage by placing infant victims on diets low in phenylalanine until they are eight to 10 years old. The development of simple urine and blood tests to diagnose the condition quickly followed.

Most states now have mandated PKU testing for all children shortly after birth, with dramatic results. For example, a recent survey of nine state mental hospitals in the West showed no children with PKU under age six, but revealed 25 patients with the disorder over age 12 who had been born before screening and treatment were available.

Unfortunately, very few genetic diseases are amenable to treatment. The immediate hope for management is the identification of carrier persons, so that families at risk for certain diseases can be informed of the risk and take measures to prevent birth of defective children. This involves genetic counseling, which is emerging as an important new preventive service.

A more desirable solution would be development of long-lasting, simply-administered treatments to counter the effects of the defective genes. This is an important long-range research goal.

Conceivably, many gene-enzyme diseases could yield to enzyme-replacement therapies if ways could be found to synthesize and deliver needed enzymes to target cells and organs.

Still other prospects, as yet relatively unexplored, lie with possibilities to transplant tissues of normal cells, if not whole organs, to perform needed

(more)

metabolic chores within the body.

Inherited defects expressed by unstable structural proteins may be managed by stabilizing drug therapies. Replacement therapies could also apply here, as is indeed now done in the supply of antihemophilic blood factors to hemophilia patients.

#

PERIODONTAL DISEASE--Periodontal disease, an insidious disorder, is the main cause of tooth loss in adults. The National Institutes of Health is making a special research effort to combat periodontal disease.

PESTICIDE EXPOSURE--The exact health effects of exposure to certain pesticides are being studied by the National Institutes of Health. Other environmental health problems are also under investigation.

AUTOMATED LABS--Medical diagnostic methods and services can be improved by automating certain laboratory processes, according to the National Institutes of Health.

Photo Feature

Women in Research...

DRS WOMEN ASSIST WITH NIH INTRAMURAL RESEARCH

Medical illustrator Marsha Jessup completes a schematic drawing illustrating the migration patterns of ectoderm and mesoderm derivatives of a chick embryo's head. Ms. Jessup, of the Medical Arts and Photography Branch, Division of Research Services (DRS), prepares all types of visuals for medical education in line, halftone, and color and also constructs three-dimensional models from some of her drawings. (NIH Photo #1158)

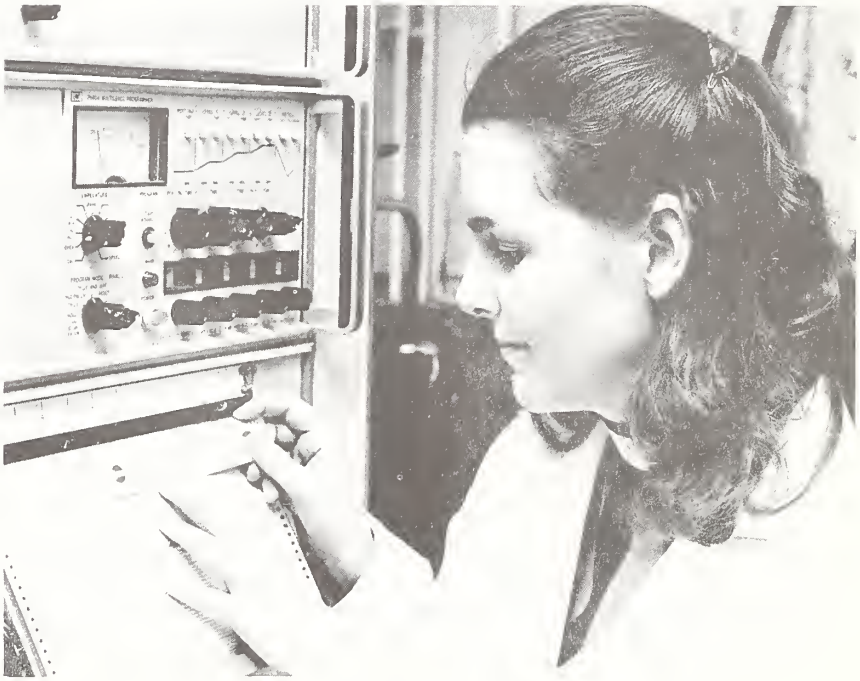
Cathy Clifford, library technician at the NIH Library, DRS, is helping one of many researchers locate a journal in the collection. Ms. Clifford receives and answers telephone inquiries about journals, books, and authors. She assists readers in using the card catalog, locating books and journals, and compiling bibliographies. She also uses the Medline Terminal for processing references to scientific publications. (NIH Photo #1159)

(more)

DRS Women (Cont'd)

Catherine Neely, a biological technician with the DRS Veterinary Resources Branch, trims tissue sections for preparation of microscope slides. Ms. Neely processes many types of animal tissue such as bone, brain, heart, liver, and muscle using two staining techniques. Requests to DRS for slides come from all parts of the country. (NIH Photo #1160)

Chemical engineering student trainee Becky Munroe checks a reading on a chemical analysis. Working with scientists in the DRS Biomedical Engineering and Instrumentation Branch, Ms. Munroe is assisting in several investigations, including a study of the kinetics of tygon tubing, a multicomponent plastic which is used in surgery as a connective system. (NIH Photo #1161)



DRS Women (Cont'd)

Pathologist Dawn Goodman, DVM, of the DRS Veterinary Resources Branch, separates an animal heart from the trachea and lung for tissue trimming and preparation of microscope slides. Dr. Goodman will study the slides to determine the exact cause of death. Her findings will then be compiled in a detailed report which, in turn, will be cross-referenced for further use by other investigators. (NIH Photo #1162)

In the DRS Glassware Unit, Mary Virginia Dietz can inspect, cover, and package 4,800 centrifuge tubes in three hours. Ms. Dietz assists in maintaining an adequate stock of all types and sizes of scientific glassware ranging from Erlenmeyer flasks, screwcap tubes, graduates, pipettes, and beakers to mortars and pestles for NIH researchers' needs. (NIH Photo #1163)

#

Medical News Tip

PARASITIC ROUNDWORM DISEASES--The National Institute of Allergy and Infectious Diseases (NIAID) conducts and supports research on the causes, cures, and control of many parasitic diseases.

Roundworm (nematodes) are a group of invertebrates with elongated cylindrical bodies. They range in size from those plainly visible with the naked eye to those only several hundredths of an inch long.

Some of the most common parasitic roundworms are: pinworms, probably the most common roundworm parasite in temperate climates; common hookworms; trichina worms which cause trichinosis; and ascarids, giant intestinal roundworms.

The ascaris worm ranges in length from 6 to 13 inches. The female worm may grow to be as thick as a pencil. Ascaris infections are common throughout the world. They are often the result of eating food which is grown in soil fertilized with human excrement, and then eaten without being properly washed.

When the ascaris eggs are swallowed and pass into the intestine, they hatch into larvae and then begin their odyssey through the body. Once through the intestinal wall, they reach the lungs by means of the blood or lymphatic system. When the larvae reach the lungs, they pass through the air sacs, climb the bronchial tree and are reswallowed to be returned to the small intestine where they grow, mature, and mate. The worms reach maturity in about two months.

For additional information about parasitic roundworm diseases, contact: NIAID Information Office, Bldg. 31, Room 7A-32, NIH, Bethesda, MD 20014, Phone (301) 496-5717.

#

Capsules

RESEARCH ILLUSTRATED

This baby Cynomolgus monkey seems to be as reluctant to read the scale as we fellow primates are. However, he weighs less than one pound and is therefore hardly pudgy. This weigh-in is part of a National Institute of Child Health and Human Development study of aging. (NIH Photo #1164)

#

New Publication:
Immunology Research--An Introduction

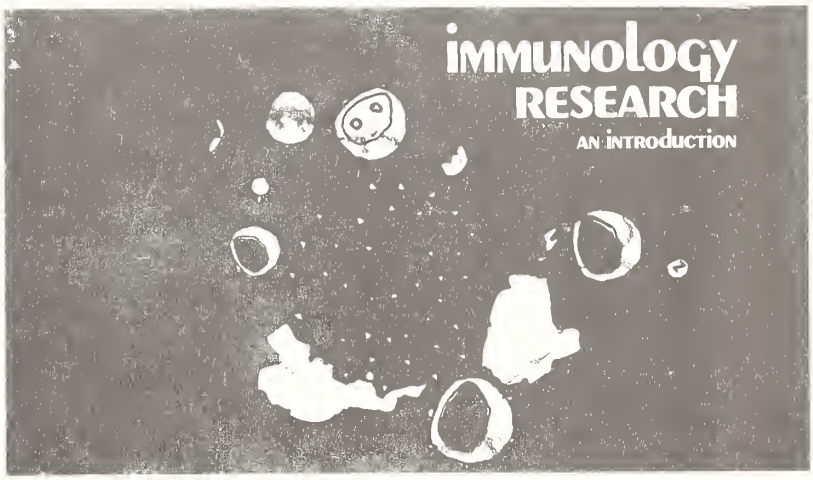
A new publication, *Immunology Research--An Introduction*, has been prepared by the National Institute of Allergy and Infectious Diseases (NIAID) to introduce the public to results of this research, particularly as they may be applied to control of a disease process.

For years, immunology research has been part of the NIAID programs, since prevention or cure of both allergic and infectious diseases is dependent upon a thorough understanding of how the body protects itself against "foreign invaders." In infectious diseases, these invaders include bacteria, viruses, or parasites; in allergic reactions, almost any substance--foods, pollens, dust--can cause trouble in a sensitized individual.

It has become increasingly clear, through research advances, that immunology plays a role in many diseases, including cancer. Therefore, several components of the National Institutes of Health support immunology studies.

Science writers can obtain a free copy of this publication from:

NIAID Information Office
Building 31, Room 7A-32
Bethesda, MD 20014
Phone (301) 496-5717



News Releases Issued

(Summaries of NIH news releases sent out since the last issue. For a copy of any of these, please write or call.)

CABLE TELEVISION--A contract has been awarded to the Mount Sinai School of Medicine, New York City, to explore the use of two-way cable television in helping old people to take care of their health. The project is being coordinated by the National Library of Medicine. Operating on the assumption that older people rely on television as an important means of receiving information, a cable television system will be used to establish two-way communication between a high-rise public housing building in East Harlem and the Mount Sinai Medical Center. The two-way communication will allow the tenants to participate in discussions and ask and respond to questions posed over the channel as well as permit the medical personnel at the Medical Center to monitor and record the progress of patients at home.

#

Editors of publications may request glossy prints of numbered photographs that appear in the regular issue.

NEWS & FEATURES From NIH
National Institutes of Health
Building 31, Room 2B-10
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November 25, 1973

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NEWS & FEATURES From NIH November 25, 1973

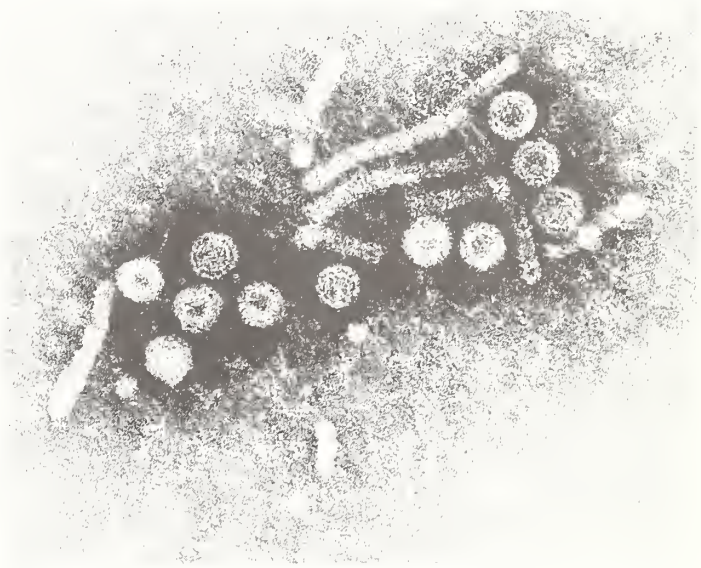
Research Advances

EVIDENCE POINTS TO DANE PARTICLE AS ELUSIVE HEPATITIS B VIRUS

Scientists supported by the National Institutes of Health and the Atomic Energy Commission (AEC) may have found the elusive virus that causes human serum hepatitis. Serum hepatitis causes 6000 deaths a year, primarily people who have received infected blood products during transfusions.

Scientists have long suspected that serum hepatitis is caused by a virus which can be transmitted from person to person by infected blood materials. Now, the NIH-supported scientists have found evidence that the agent which causes serum hepatitis contains nucleic acid, the genetic material for many viruses and other organisms, including man. This is the first clue that the agent has one of the most important attributes of a conventional virus. Until this time, the virus itself had never been isolated and cultivated in living cells, nor had scientists shown conclusively that it contains nucleic acid.

These findings are important if a vaccine is to be developed to prevent the disease. More immediately, the finding could lead to a better test for detecting infectious blood and blood products, which could cut down on the incidence of illness and death caused by the disease.



The Dane particles and filamentous form of hepatitis B antigen are shown at a final magnification of 150,000x. (NIH Photo #1165)

(more)

Dane Particle (Cont'd)

For several years, scientists have known that a foreign substance, or antigen, is associated with serum hepatitis (also called hepatitis B). In the sera of hepatitis patients or carriers this antigen exists in three physical forms: a small sphere; a filamentous form; and a larger, more complex particle having an outer coat and a smaller inner core. The complex form is called the Dane particle after the British investigator who first described it in 1970.

Since the Dane particle's appearance is similar to that of a virus, scientists have been trying to detect associated nucleic acid or some other marker of viral activity which could confirm that the particle is the long-sought-after hepatitis B virus. The NIH-supported team of scientists found just such a marker--an enzyme called DNA polymerase which directs the synthesis of deoxyribonucleic acid (DNA), one type of nucleic acid.

Using the electron microscope, scientists at the Molecular Anatomy (MAN) Program Laboratory, sponsored jointly by the National Institute of Allergy and Infectious Diseases (NIAID) and the AEC, first examined plasma samples from chronic carriers of hepatitis B antigen. John L. Gerin, Ph.D., of the MAN Laboratory selected eight patients whose sera had relatively high concentrations of Dane particles. The sera from these individuals were then concentrated and purified by Dr. Gerin.

Working with these preparations, a team of scientists at the Stanford University Medical School detected DNA polymerase activity in each of the eight sera. In contrast, the Stanford researchers were unable to detect any DNA polymerase activity in seven samples of sera from people who did not have hepatitis B antigen.

(more)

Dane particles (Cont'd)

From other experiments, the investigators determined that the core of the Dane particle most likely contains a DNA "template" which directs the synthesis of DNA.

These findings, although indirect, suggest that the Dane particle is the human hepatitis B virus that scientists have been seeking for so long and that the virus itself is a DNA virus. This research could lead to development of a better test for infectious blood and blood products--for example, one in which polymerase activity would be a marker of infectivity. Currently, screening tests for hepatitis B rely upon detection of hepatitis B antigen.

In addition, identification of the Dane particle as the virus of hepatitis B would be an important step in development of a vaccine, since, traditionally, isolation and growth of a virus in tissue culture is a vital prerequisite.

This research was carried out by Paul M. Kaplan, Ph.D., William S. Robinson, M.D., and Richard L. Greenman, M.D., of the Stanford University School of Medicine; Dr. Gerin of the MAN Laboratory, Rockville, Maryland; and Robert H. Purcell, M.D., of NIAID's Laboratory of Infectious Diseases. (Dr. Kaplan is now at the MAN Laboratory.) In addition to NIAID and AEC support, the scientists received funds from the National Cancer Institute, the National Institute of Arthritis, Metabolism, and Digestive Diseases, and the Damon Runyon Memorial Fund. A report of the research was published in the November 1973 issue of *Journal of Virology*.

#

NEWS & FEATURES From NIH November 25, 1973

Research Advances

HOSPITAL NOISE LEVELS PRESENT HEALTH HAZARDS

Hospital noise levels in infant incubators, recovery rooms, and acute-care units are of sufficient intensity to interfere with sleep and possibly damage hearing in some patients.

According to Stephen A. Falk, M.D., of the National Institute of Environmental Health Sciences, studies show that these noise levels probably stimulate the pituitary-adrenal axis of patients, exceed the noise threshold for peripheral vasoconstriction, interfere with sleep, and pose a threat to hearing in patients receiving aminoglycosidic antibiotics.

Dr. Falk and Nancy F. Woods, R.N., of the Duke University School of Nursing, attempted to identify the sources and measure the levels of excessive noise present in a hospital and to relate these levels to possible patho-physiologic effects on the hospitalized patient.

The investigators made 24-hour measurements with a sound level meter of the sound pressure levels in functioning infant incubators, a 17-bed surgical recovery room, and two rooms of a 7-bed acute-care unit (for cardiac surgery).

They chose the recovery room and acute-care unit for noise measurements because these are considered to be the noisiest patient areas in the hospital. Incubators were included to determine whether cases of childhood deafness of unknown cause could be attributed to this source. Additionally, the investigators considered patients in these three areas to be at greatest risk from the potential hazardous effects of noise.

(more)

Noise (Cont'd)

Each incubator was analyzed twice without the infant by measuring sound where the child's head would normally rest. The investigators measured background noise for each incubator with the incubator not functioning and compared this with noise levels obtained with the incubator in a normally functioning situation. The study revealed the source of the noise to be the electric motor and fan below the infant compartment of the incubator.

Noise levels in the recovery room and acute-care unit were measured by placement of the microphone as close to the heads of the patients as possible to record sound levels to which patients are routinely exposed. The predominant sources of noise were mechanical equipment, personnel, and procedures.

In the recovery room, the mean noise level was higher during the day than at night. There appeared to be a significant association between noise and the number of patients. Also, the investigators found a significant correlation between noise and the number of staff at the bedside in both the recovery room and acute-care unit. The major contribution of personnel to the observed noise levels was from their conversation, which was often "needlessly loud" and not directly related to patient care.

According to Dr. Falk, these findings show that physicians must consider noise to have possible detrimental effects on human health, especially on the health of hospitalized patients. He explains that while there is no known noise-induced disease other than deafness, noise does produce well-recognized physiologic changes in the endocrine, cardiovascular, and auditory systems in addition to effects on sleep.

(more)

Noise (Cont'd)

The pituitary-adrenal axis has an extremely low threshold for stimulation by noise--as low as 68 decibles (linear). According to Dr. Falk, the average noise levels in the recovery room, acute-care unit, and incubators exceeded this intensity. It seems highly probably to him, therefore, that noise levels as measured in this study stimulate the pituitary and adrenal systems of hospitalized patients. Noise can therefore be considered a nonspecific stress that releases ACTH from the pituitary. "Since these patients are already in stressful situations from multiple causes," he explains, "it seems wise to decrease any further stress to which they are exposed."

On the basis of present knowledge of the cardiovascular effects of noise, Dr. Falk concludes that the average noise levels of 69.8 decibles (linear) in the recovery room and 73.3 decibles (linear) in the acute-care unit (room 1) approximately equal and exceed respectively the threshold of 70 decibles (linear) for constriction of the peripheral blood vessels. Such vasoconstriction, he explains, is a well-established effect of noise on the human cardiovascular system.

In addition to vasoconstrictive effects in the periphery, noise produces similar changes in the ear and placenta. Noise-induced vasoconstriction of spiral vessels causes noise-induced hearing loss in humans. Exposure of rats to chronic noise produces abnormalities of fetal development and a decrease in litter size. The noise causes a decrease in placental blood flow and the resultant hypoxia alters normal fetal development.

Laboratory animal studies have also demonstrated elevated plasma cholesterol and increased atherosclerosis and ventricular hypertrophy after

(more)

audiogenic stimulation. Whether similar changes can occur in human subjects is unknown. Retrospective studies have indicated a greater prevalence of cardiac and peripheral vascular disease and hypoglycemia in workers in very noisy industries than in people in less noisy industries. However, Dr. Falk explains, firm conclusions cannot be made from these studies because they did not control for work conditions.

Dr. Falk also believes that the noise levels observed in the present study may be dangerous to patients being treated with aminoglycosidic antibiotics.

Recent laboratory studies demonstrating potentiation of the damaging effects of noise and ototoxic aminoglycosidic antibiotics can be applied to hospitalized patients. These studies show a tremendous amount of hair cell damage on exposure to kanamycin and noise levels of 58 decibles (A-weighted) as compared to exposure to either agent alone. The amount of damage greatly exceeds that expected from the addition of the separate effects of each agent. According to the investigators, a similar level of noise is also present in the incubators, recovery room, and acute-care unit in the present study.

Hospitalized patients are also at a greater risk of impaired hearing from noise because of continuous exposure (more damaging than the intermittent exposure in everyday life) and the lack of opportunity for recovery.

Noise levels in the present study are incompatible with normal sleep, Dr. Falk says, because they almost always exceed 50 decibles (A-weighted), a level that has a 25 percent probability of seriously affecting sleep. Noise

(more)

Noise (Cont'd)

appears to be one of the many factors contributing to sleep deprivation of patients in an intensive-care unit.

According to the investigators, insufficient data make it impossible to set strict criteria for hospital noise levels that will not adversely affect cardiovascular or endocrine functions. Until such criteria can be set, they offer suggestions for the medical and nursing staff to decrease noise levels:

The high correlation between noise levels and the number of staff at the patients' bedside suggests that personnel make a special attempt to limit unnecessary conversation.

Patients who are being treated with aminoglycosidic antibiotics should not be exposed to an average noise level greater than 58 decibles (A-weighted).

All noise-producing devices should be positioned as far from the patients' heads as possible.

A distance should be maintained between patient beds by not filling two adjacent beds unless it is essential. Also, patients should be first assigned to beds not contiguous with work areas such as the nursing station.

Patients in intensive care and acute-care units should ideally be placed in individual cubicles designed for noise reduction.

Patients can be given earplugs for sleeping.

The investigators published the results of this research in the *New England Journal of Medicine*, October 11, 1973. Dr. Falk previously published results of a study of incubator noise and deafness in *Archives of Otolaryngology*, May 1973. A report of this work appeared in the June 25, 1973 issue of *NFFN*.

#

Research Advances

DIFFERENCES IN COLLAGEN MAY EXPLAIN OSTEOARTHRITIS

The metabolic differences recently identified between normal and osteoarthritic human collagen help explain the nature of the degeneration of cartilage in the joints seen in this disease. Collagen is the chief connective tissue protein of the body.

This finding, reported by Marcel Nimni, Ph.D., and Kalindi Deshmukh, Ph.D., of the University of Southern California School of Medicine, Los Angeles, offers a clue that may help scientists figure out the cause of the crippling condition. Osteoarthritis, a degenerative disease of the joints, is characterized by cartilage destruction in joints exposed to maximal mechanical stress, especially the weight-bearing joints.

In 1969, Edward J. Miller, Ph.D., and Victor Matukas, D.D.S., Ph.D. (both working at the National Institute of Dental Research (NIDR) at the time), discovered that cartilage collagen differs significantly from skin and bone collagen. The investigators suggested that the particular configuration of cartilage collagen might be essential for the structural integrity of the tissue.

Cartilage, which lines the hip and other joints where the bones meet (articulate), must withstand tremendous mechanical stress from such normal activities as walking, carrying, and running.

Dr. Miller and Matukas found that cartilage collagen is assembled from three identical chains and that the chain which he then termed $alpha_1$(II) differs from the $alpha_1$ chain in skin and bone (subsequently renamed $alpha_1$(I)). Skin and bone collagen contain two $alpha_1$(I) chains and one $alpha_2$ chain.

(more)

Collagen (Cont'd)

With grant support from NIDR and the National Institute of Arthritis, Metabolism, and Digestive Diseases, Drs. Nimni and Deshmukh compared the collagen from human osteoarthritic joints with that of normal articular cartilage. The tissue samples were taken during surgery from patients whose arthritic joints were replaced with implants and from non-arthritic patients who required bone surgery.

The investigators found that while normal cartilage collagen contains only $alpha_1$(II) chains, diseased joint tissue additionally synthesizes significant amounts of $alpha_2$ chains and the corresponding beta components. Therefore, as a result of this disease, a tissue which usually synthesizes three chains of $alpha_1$(II) collagen exclusively will synthesize the more general (skin and bone) type of collagen containing the $alpha_2$ chain.

Drs. Nimni and Deshmukh published these findings in *Science*, August 24, 1973. Preliminary findings by these same investigators published in *Biochemical and Biophysical Research Communications* suggest that lysosomal enzymes, which are significantly increased in osteoarthritis, may play a major role in the development of such an abnormality. In these experiments, they found that normal bovine articular cartilage, which only synthesizes $alpha_1$(II) collagen chains, begins to synthesize $alpha_2$ chains after pre-incubation of the tissue with rat liver lysosomal enzymes.

Although the mechanisms underlying changes in metabolic patterns are unknown, it appears that substitution of the $alpha_2$ chain for the $alpha_1$(II) chain in osteoarthritis generates a different collagen fiber which may not function as well as cartilage collagen and therefore lead to joint damage.

(more)

Collagen (Cont'd)

NIDR is engaged in collagen studies because the chemistry of connective tissue protein is important in understanding the physiology of the periodontium (which includes gingiva, two supportive fibers, and bone).

#

DEAFNESS--Heredity has been found to be a large factor in the cause of deafness. About half of the deaf children in this country have a hearing loss from hereditary factors, and about one-third of adults who develop deafness are deaf from hereditary causes, according to the National Institutes of Health.

EPILEPSY--Epilepsy is not contagious, according to the National Institutes of Health. There is only a little evidence to suggest that some rare types, or susceptibility to some types, are hereditary.

EPILEPSY CONTROL--So far, the most successful control of epilepsy symptoms is with drugs, according to the National Institutes of Health .

Photo Feature

After Exposure to Light...

SYNTHETIC DYES KILL HOUSEFLIES

Houseflies at the West Virginia University Agricultural Experiment Station die by the score after eating any of several synthetic dyes and then being exposed to light.

Linda Butler, Ph.D., and Timothy P. Yoho, Ph.D., find that some synthetic dye compounds used extensively in industry are deadly to the common pest. Dr. Butler's research is supported by the National Institute of Allergy and Infectious Diseases.

The key to the fatal action lies in the photodynamic action of some of the dyes tested thus far. Flies that eat certain dyes mixed in a milk-sugar bait die within one to three hours after they are exposed to light. On the other hand, flies that eat the same dyes but remain in darkness show no ill effects.

Photodynamic activity created by light falling on certain dyes apparently changes their harmless chemical structures to structures which cause destructive changes when the dyes are associated with other chemicals found in living cell tissue or body fluids like the blood.

The common housefly has a relatively transparent body structure which allows light to penetrate the outer part of the body and reach the internal organs. Light, therefore, reaches any place where dyes might locate within the body after they have been ingested by the insect. (NIH Photo #1166)

(more)

Houseflies (Cont'd)

Researchers Linda Butler, Ph.D., and Timothy P. Yoho, Ph.D., of West Virginia University, study houseflies in experimental cages to determine whether commercial dyes have killed any of the flies. (NIH Photo #1167)

Although he has yet to discover just how certain dyes act in the insect's body to kill it, Dr. Yoho believes the answer may be found in the complex nerve system. (NIH Photo #1168)

The investigators have found that dyes which contain a xanthene chemical structure appear to be most active in the tests. Also, the most effective dyes are those of yellow, orange, or red colors. The active dyes seem to be working most heavily on some part of the nervous system.

"Instead of dying simply and suddenly, the insects go through a very active period, then apparently lose coordination of body parts before they die," observed Dr. Yoho. "These are classic symptoms of nerve poisons."

While the research team's primary interest is learning something about the basic action of dyes on parts of the insect body, the practical application of its findings would be an insecticidal treatment.

#

NEWS & FEATURES From NIH November 25, 1973

News Feature

TOOTH DECAY AFFECTS MAJORITY OF AMERICANS

Tooth decay causes pain and other ill effects in 95 percent of the people of this country. One of the most common causes of pain and debilitation in children, also often causes distress in adults.

In a survey of nutritional conditions in low-income areas conducted by the Public Health Service a few years ago, about one-fifth of all subjects 10 years of age and over reported difficulty or pain when biting or chewing food. Extensive decay was widespread throughout the group.

Those in less favored economic circumstances are particularly subject to the ravages of dental caries because these people often cannot or do not seek help. Since this disease is not self-limiting, any neglect creates fresh problems.

The deficit in care is borne out by a comparison of visits to the dentist made each year by children in low- and high-income families. Only one-fourth of the children in families with under $5,000 income see a dentist at all during the year, as contrasted with over two-thirds of those in the over $15,000 income group.

Scientists involved in the National Caries Program of the National Institute of Dental Research (NIDR) recognize that there is no single solution to the problem of tooth decay. Therefore, they are directing attention to the three factors believed to be responsible for this disease.

One major focus of research is to strengthen the resistance of teeth to the destructive action of acid produced in the mouth. Water fluoridation

(more)

Tooth Decay (Cont'd)

represents the greatest preventive measure in dentistry and is, in fact, one of the most effective in the entire field of health. Through its scientific studies, NIDR has established the benefits and safety of this technique and is now seeking other means to increase the 60 percent reduction in tooth decay effected by water fluoridation.

In another approach, scientists are trying to reduce the levels of harmful oral bacteria and their products that attack the teeth. Still other research is directed at counteracting or eliminating sucrose in the diet. One current study, for example, is searching for a palatable carbohydrate to substitute for sugar in snack foods and desserts.

Special emphasis is being placed on studies of the bacterial film called plaque that forms on the teeth and gums. Held fast to the teeth in plaque, acid-producing bacteria can wreak havoc in the mouth. By diligently following good practices of oral hygiene (including careful brushing as well as flossing between the teeth), cutting down on sweets (particularly in-between-meal snacks since frequency of eating appears to be a factor), and seeing a dentist regularly for professional care, most people can have better dental health.

At present, Americans spend over $2 billion a year to treat caries. It is estimated that if all new cavities which occur each year were to be filled, the cost to Americans would be over $10 billion. To help resolve the problems of cost and limited availability of professional care, the National Caries Program is searching for more practical and effective ways of lowering the incidence of tooth decay.

#

Photo Feature

NIAID WORKING TO DEVELOP IMPROVED CHOLERA VACCINE

The monsoon winds have lessened in Bangladesh, but the incidence of cholera has greatly increased. Cholera outbreaks are expected from October until the rains begin again in May.

Because the current vaccines against cholera provide only short-lived protection, an international effort is underway to improve the vaccines.

The National Institute of Allergy and Infectious Diseases (NIAID) is developing a cholera "toxoid" from purified toxin to learn if this should

(more)

After this Hindu woman received a new cholera toxoid, a physician checks the injection site regularly for redness and swelling. She will receive a booster shot six weeks after the first injection. NIAID is participating in an international effort to develop a better cholera vaccine. (NIH Photo #1169)

Cholera (Cont'd)

be an ingredient in the ultimate vaccine. This toxoid is now being tested in a group of 270 people in the Matlab region of Bangladesh.

This early trial, conducted by the Cholera Research Laboratory of the Institute of Public Health in Dacca, may lead to a field trial among 100,000 people beginning in late 1974. Scientists hope to learn whether antibody induced by this toxoid will protect people living in an endemic area against cholera diarrhea.

Carl E. Miller, D.V.M., NIAID cholera project officer, recently visited the Laboratory (and took the photographs in this feature).

Supporting the Laboratory are NIAID, the Center for Disease Control, the Agency for International Development, and the governments of Bangladesh, Great Britain, and Australia.

(more)

A shipment of jute heads toward a market in Matlab, a region of Bangladesh. The men delivering this fiber are part of a small group testing a new cholera toxoid preparation. If results of the current study are encouraging, a larger study of 100,000 people will begin in late 1974. (NIH Photo #1170)

Cholera (Cont'd)

These Bangladesh schoolboys are returning home along a path that was partially flooded by monsoon rains. An international effort is under way to help protect local people from Cholera outbreaks. (NIH Photo #1171)

#

GAMMA CAMERA--National Institutes of Health scientists use a gamma camera linked to a computer to evaluate the surgical repair of heart valve defects.

Medical News Tip

MALARIA RESEARCH--One approach to the problem of controlling malaria involves biological control of malaria-carrying mosquitoes. The National Institute of Allergy and Infectious Diseases (NIAID) is using parasites and predators to kill mosquitoes. Another method is genetically manipulating mosquitoes so that they do not reproduce.

Biological methods gain importance as mosquitoes develop more resistance to insecticides. However, biological control is not yet used routinely because it is expensive and time-consuming.

NIAID grantees and other scientists have conducted a field test at the Central America Malaria Research Station in San Salvador, El Salvador. Sterile male Anopheles mosquitoes were released in large numbers in breeding areas around a lake. The sterile males "mated" with normal females but produced no offspring. Soon the lake was free of malaria-carrying mosquitoes.

For additional information, contact:

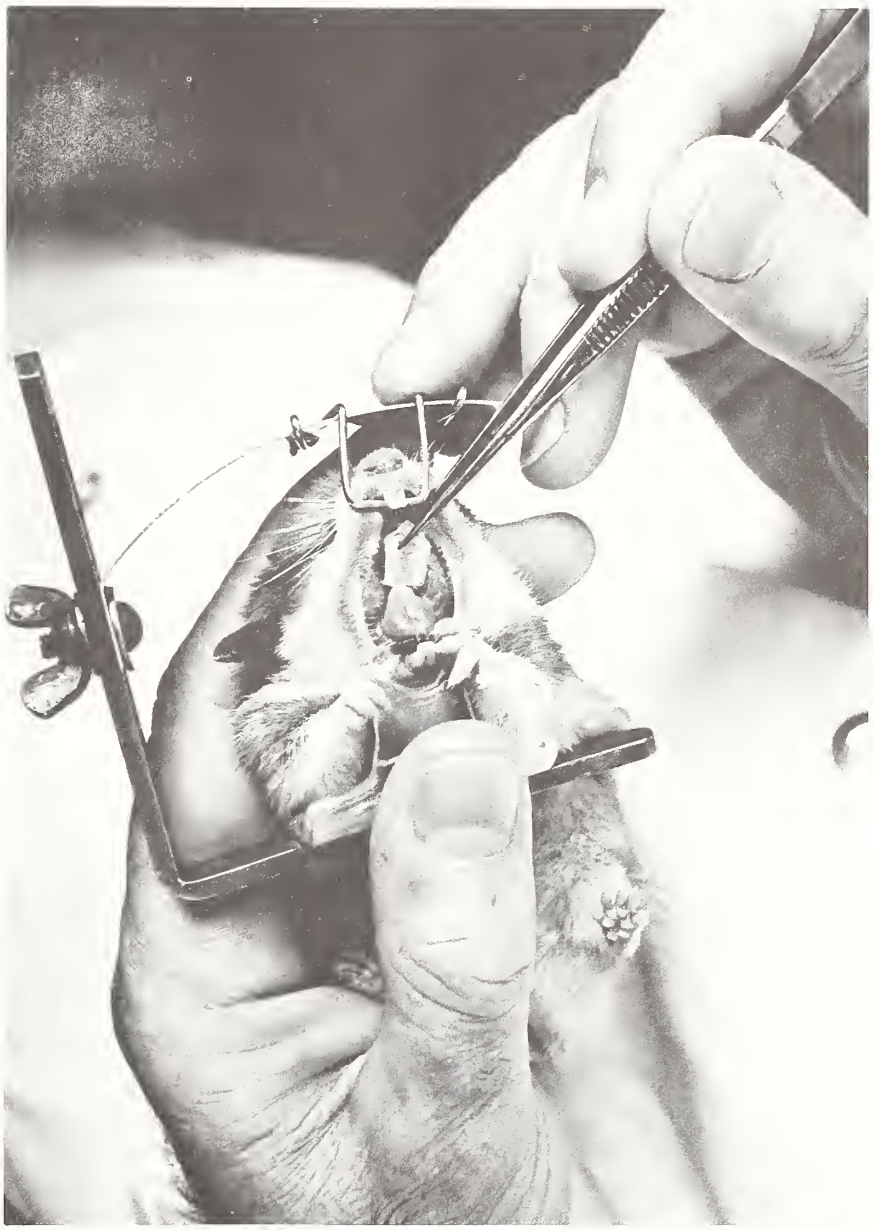
NIAID Information Office
Building 31, Room 7A-32
NIH, Bethesda, MD 20014
Phone (301) 496-5717

#

ROOT DECAY--About 40 percent of American adults have at least one tooth with root decay, reports the National Institutes of Health.

Capsules

Research Illustrated



This hamster, which was born in a germfree chamber at the National Institutes of Health, is exposed to a single form of tooth decay-causing material. Scientists at the National Institute of Dental Research then study how one form of bacteria affects its teeth. (NIH Photo #1172)

#

New Publication:
Food Allergy

Eating is something most people do almost without thinking. To some, however, a single bite of the wrong food can bring on the unpleasant, and sometimes frightening, symptoms of food allergy.

A familiar allergic reaction to food is the itchy rash some get after eating strawberries. To others, food allergy may manifest itself in a gastrointestinal upset, a wheezing asthma attack, sneezing and runny nose of allergic rhinitis (hay fever), or the scaling, itching skin of allergic eczema.

The National Institute of Allergy and Infectious Diseases (NIAID) has released a new publication, *Food Allergy*, dealing with the causes, symptoms, and treatment of allergic reactions to foods.

The mechanism of food allergy does not differ from that of allergies to inhaled substances. However, because changes can occur in environmental factors, diet, and body chemistry, food sensitivities sometimes disappear during an individual's lifetime. But, the allergic state or tendency remains.

Science writers can obtain a free copy of this publication from:

NIAID Information Office
Building 31, Room 7A-32
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#

News Releases Issued

(Summaries of NIH news releases sent out since the last issue. For a copy of any of these, please write or call.)

CONGENITAL ABNORMALITIES--The National Institute of Child Health and Human Development will provide funds for the computer monitoring of about one million births per year to provide early warnings of unusual frequency or association of congenital abnormalities. More than 1500 hospitals in the United States will be asked to provide information to the birth defects monitoring program. The program will be directed by the Center for Disease Control in Atlanta.

#

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December 10, 1973

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There will be no December 25 issue of NEWS & FEATURES From NIH. Publication will resume on our usual twice-monthly schedule with the issue dated January 10. Best wishes for the holiday season and the coming New Year.

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NEWS & FEATURES From NIH December 10, 1973

Research Advances

CHIMP COMMUNICATES WITH COMPUTER

Language skills may not be limited to humans. Recent studies reveal that a 2 1/2-year-old female chimpanzee in a computer-controlled training situation can both read the beginnings of familiar sentences and appropriately complete them for reward or reject them when incorrect.

Lana, a chimpanzee at the Yerkes Regional Primate Research Center, Emory University, Georgia, talks in "Yerkish". The center is supported by the NIH Division of Research Resources. The National Institute of Child Health and Human Development provides funds for these studies.

Investigators Duane M. Rumbaugh, Ph.D., and Timothy V. Gill conducted four experiments with Lana to determine whether, after six months of language training, she was capable of reading sentence beginnings and thereby capable of discriminating between those that were valid and those that were invalid.

The language training equipment for the experiments includes: a console holding 25 word keys; a row of seven rearview projectors for visual display of communications; a device that opens a window for viewing the outdoors. A computer monitors Lana's performance, controls a teletype that records the experiments, and dispenses the various incentives that the chimp requests--such as food, candy, liquids, music, movies, and toys.

A second console, accessible only to the researchers, allows them to initiate selected word chains (sentences). The console allows for alterations in the position of keys so that the location of a key would not reliably indicate its meaning. The Yerkish words (or lexigrams) used on the console consist of distinctive white geometric symbols on colored backgrounds.

(more)

Chimp (Cont'd)

Each sentence formed by the chimp must be ended with the depression of the period key, which signals the computer to evaluate the communication. If the communication is incorrect, the computer erases the projected images and resets the keys. If the communication is acceptable, the computer activates the dispensing or control unit appropriate for the requested incentive or event.

Initially, the investigators trained Lana to press single keys to request various incentives. Following that, she learned to precede each request with *please* and follow it with a *period*. The third stage of training consisted of learning to press any key of a holophrase (composed of symbols on separate keys in the correct order)--for example, *machine give M&M*--and

(more)

Lana's computer-controlled language training situation is shown in the photo at right. The overhead bar must be pulled to activate the console. Facsimiles of the lexigrams on the surfaces of the word keys are portrayed on the projectors above the keyboard, from left to right, as she presses the keys. Shown on the projectors is please machine give piece of banana. *Lana is about to press the period key. Juice and water dispensers are immediately below the console; the banana and candy dispensers are shown at the lower right. (NIH Photo #1173)*

then learning to use *please* and the *period*. The chimp next learned to press any key for each part of a fractionated holophrase--such as *machine give/ M&M*, with *please* and *period*. Then, the chimp pressed each key of a correctly ordered series of words once treated as a holophrase--for example, *please/ machine/give/M&M/period*.

Lana also learned to press the keys in the correct order with the linear sequence of keys randomized; finally, she selected and depressed the keys in the correct sequence, even with the keys randomly assigned among others on the console.

The results of the four experiments present evidence that Lana accurately perceives Yerkish words, reads their serial order, and discriminates whether they can or cannot be completed to obtain the various incentives. The investigators believe that their experiments did assess perceptual process because Lana had to attend to the serial order of lexigrams as well as to their meanings. Lana's reading was inferred from the accuracy with which she successfully completed sentences that were validly initiated and appropriately rejected.

The researchers conclude that the probability of Lana being correct by chance on any one trial of the first two experiments was less than 10 percent. The fact that she was 95 percent correct overall makes chance an unlikely determinant of her performances.

According to the investigators, if the successful completion of the valid sentence starts can be viewed as analogous to typewriting, then Lana both "reads" and "writes". They admit, however, that they have no evidence

(more)

of her ability for arithmetic.

A complete report of the experiments with Lana appears in *Science*, November 16, 1973.

#

IMMUNE SYSTEM--A human's immune system usually protects the body, but sometimes the system goes wrong and leads to immunodeficiency diseases. The National Institutes of Health is studying many aspects of immunology.

TOOTH ROOTS--As long as they are hidden by the gums, tooth roots are usually well-protected from plaque and decay. However, when the gums recede, decay can be a big problem, according to the National Institutes of Health.

SEIZURES--About 75 percent of people who are susceptible to epileptic seizures can now have at least 75 percent of their attacks prevented, and many of these remain seizure-free for years if their treatments (drugs, or surgery and drugs) are properly maintained, according to the National Institutes of Health.

Research Advances

Animal Model...

LEAD POISONING LINKED TO HYPERACTIVITY IN MICE

Chronic ingestion of lead can produce a significantly increased level of motor activity in mice. This recent finding strengthens the evidence that a similar link exists between lead poisoning and minimal brain dysfunction, or hyperactivity, in children.

Ellen Silbergeld, Ph.D., and Alan M. Goldberg, Ph.D., of the Johns Hopkins University School of Public Health, exposed mice to lead from birth by substituting solutions of lead acetate for the drinking water of their mothers. After weaning, the young mice were divided into groups and maintained on various levels of lead or tap water and their behavior was monitored between 30 to 150 days of age.

The investigators report that ingestion of lead significantly increased levels of motor activity in mice. In fact, treated mice were slightly more than three times as active as controls. At 30 days of age, offspring maintained on lead solutions began to show motor deficits and the suggestion of behavioral disorders due to lead. Some of these animals developed poor coordination of their hind limbs and a characteristic splayed gait. The researchers also observed a heightened reactivity and an increased frequency of fighting among these animals. (Hyperactive children suffer from aggressiveness, irritability, and inability to concentrate.)

Drs. Silbergeld and Goldberg also report that growth and development were significantly affected in offspring of mothers given lead solutions to

(more)

drink. A dose-related depression in growth from day five through day 60 was observed in mice treated with two, five, and 10 mg/ml lead acetate. The control offspring, however, reached near control weight within 10 days after removal of lead. Such developmental landmarks as eye opening, full incidence of body hair, coordinated walking, and weaning were greatly retarded in mice receiving lead, often by as much as eight days in comparison to controls.

According to the investigators, increases in the amount of lead to which animals are exposed do not change heightened motor activity, but may induce other consequences such as lack of muscle coordination, degenerative brain diseases, and death. Animals treated with 10 mg/ml lead acetate did, in fact, begin to die by day 90.

The researchers gave the treated mice the stimulants usually prescribed to reduce the abnormal amount of activity in hyperactive children. D-amphetamine, the most widely prescribed drug for hyperactive children, reduced the motor activity of hyperactive mice by 90 percent, just as it does in children. Phenobarbitol, normally a sedative, increased the animals' activity--as it does with certain types of hyperactivity in children.

According to Drs. Silbergeld and Goldberg, their findings strengthen the theory linking hyperactivity with lead exposure in children and suggest that an increase in hyperactivity may be one of the earliest behavioral effects of lead poisoning. The study results support a causal relationship between chronic, sublethal lead exposure and a serious behavioral disorder.

(more)

Lead Poisoning (Cont'd)

The identification of the mouse as an animal model of a behavioral aspect of lead poisoning permits further investigations into neurochemical mechanisms and possible therapies. The investigators explain that lead-induced behavioral disorders appear to have significant parallels with the pharmacology of minimal brain dysfunction hyperactivity in children, thus making the model useful in the study and testing of therapeutic drugs for the disease.

Drs. Silbergeld and Goldberg reported their findings at the Conference on Low Level Lead Toxicity held on October 2, 1973 in Raleigh, North Carolina. Their work was supported by the National Institute of Environmental Health Sciences. Dr. Goldberg is also a grantee of the National Institute of Neurological Diseases and Stroke.

#

SINUS ATTACK--A "sinus attack" or sinusitis is an inflammation of one of the many hollow air spaces in the human body. The National Institutes of Health reports that nearly everyone has experienced sinusitis, usually affecting part of the head.

Research Advances

IN THE LITERATURE:
Nature, July 20, 1973

EMERGENCE OF RESISTANT STRAINS LIMITS USEFULNESS OF RIFAMPIN--Rifampin, a new kind of anti-bacterial drug, should not be used to treat large-scale chronic infections such as trachoma, according to National Institute of Allergy and Infectious Diseases (NIAID) grantees at the University of California Medical Center, San Francisco.

In experiments involving embryonated eggs, the scientists found that rifampin-resistant mutants of the organism causing trachoma, a widespread and serious infectious eye disease, appeared rapidly.

Earlier research by other investigators had suggested that the emergence of rifampin-resistant mutants of *Chlamydia trachomatis* (the trachoma agent) might be extremely rare. It was hoped, therefore, that long-term use of rifampin might eradicate the chlamydiae, rather than merely suppress disease symptoms as is the case with topical and systemic tetracycline therapy. Recurrences of the disease activity are common after tetracycline therapy, and the damage from such recurrences leads to visual impairment in millions of people.

Before putting this theory to clinical test, the California investigators decided to observe in the laboratory the rapidity with which rifampin-resistant chlamydial mutants might appear.

They used two strains of chlamydia for this research--one of which had been isolated from an American Indian child. (Recurrent trachoma is a major cause of blindness among American Indians and other population groups throughout the world.) The investigators injected solutions of the organism

(more)

and a small amount of rifampin into embryonated eggs. Suspensions of any yolk sacs which became heavily infected were transferred to new groups of embryonated eggs, along with increasing amounts of rifampin.

After five to seven such transfers, the scientists found that rifampin-resistant chlamydiae emerged rapidly. These mutants caused the death of all inoculated embryonated eggs, even in the presence of large amounts of the drug. Thus, they found that the emergence of rifampin-resistant mutants in chlamydial populations is not fundamentally different from that observed in populations of bacteria, causing diseases such as tuberculosis and meningitis.

These results suggest to the investigators that any large scale or long-term therapy of a chronic infection similar to trachoma with rifampin as the sole drug appears undesirable.

H. Keshishyan, L. Hanna, and Ernest Jawetz report the results of their research in the July 20, 1973 issue of *Nature*. Dr. Jawetz is supported by the National Eye Institute.

#

ASTHMA--Asthma is a non-contagious disease of the lungs which afflicts nearly nine million Americans. Although it can occur at any age, the disease usually shows up during early childhood, according to the National Institutes of Health.

Photo Feature

At Clinical Center...

NURSES USE UNIQUE KNOWLEDGE TO IMPROVE PATIENT CARE

At the Clinical Center, the NIH research hospital, nurses share responsibility for learning more about disease and its treatment. Because Clinical Center nurses give close attention to each patient, they are able to observe minute changes in a research patient's condition or behavior, often providing important clues to the disease process.

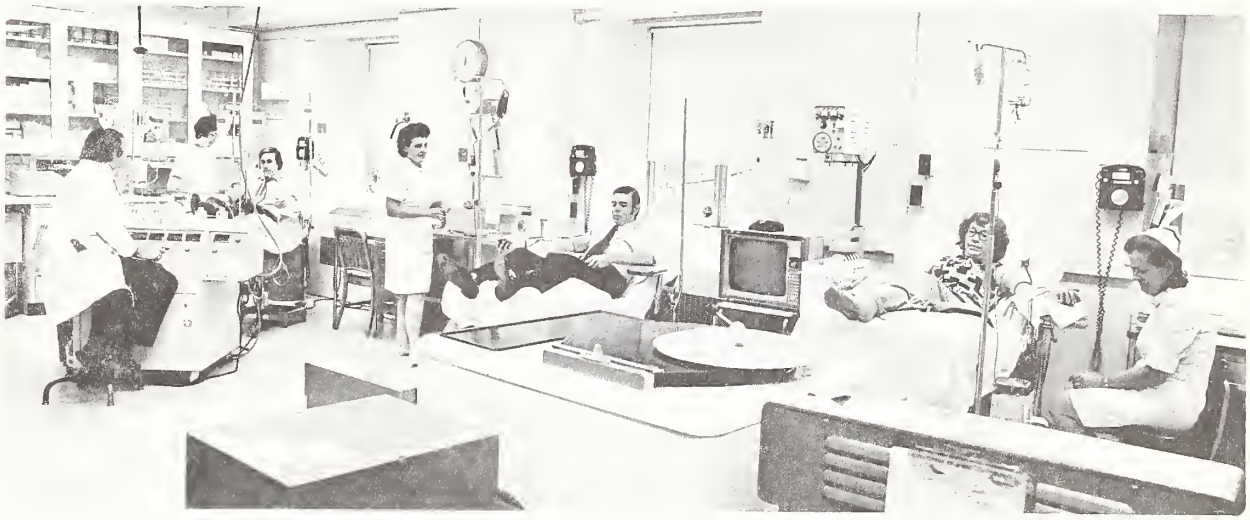
Many Clinical Center nurses have used their advanced nursing skills and thorough understanding of treatment procedures to initiate ways to improve patient care.

Clinical Center nurses are able to evaluate subtle changes in the physical and emotional health of patients. The child with nurse Jane Tolton is wearing a seizure helmet. The helmets help protect seizure-prone patients who are not on seizure-preventing medication. (NIH Photo #1174)

(more)

Nurses (Cont'd)

Nurses played a key role in design of the Clinical Center's ultramodern circular suite for heart and brain surgery. They helped develop laminar air flow rooms to protect patients especially susceptible to infection. One Clinical Center nurse devised a method for collecting 24-hour urine specimens from infants, a technique that plays an important part in research on childhood diseases.



Plasmapheresis is a relatively new method for obtaining large quantities of blood components needed at the Clinical Center for patients with hemorrhagic or immune deficiency diseases. Blood is drawn, components removed, and the rest returned immediately to the donor. Nurses Ruth Estabrook (left), head nurse Regina Dowling, and Louise Osborne (right) are alert for any unusual reactions or problems during the complicated and lengthy procedure. (NIH Photo #1175)

Since Clinical Center nurses gain unique knowledge of patients, they are included in interdisciplinary conferences and discussions.

Specialized nursing techniques used at the Clinical Center are described several times each year at clinical nursing conferences held at the hospital. The proceedings of selected conferences are published to make procedures developed at the Clinical Center available to other nurses as well.

(more)

Nurses (Cont'd)

Treatment for patients in the mental health program includes learning to deal with ordinary situations they will encounter outside the hospital, such as grocery shopping and meal preparation. Clinical Center psychiatric nurses like head nurse Sylvia Beal (right) wear regular clothes rather than uniforms to help create a home-like atmosphere. (NIH Photo #1176)

Men are an essential part of the nursing team. Max Gearhart is chief of the Psychiatric Nursing Service at the Clinical Center. Here he demonstrates the use of a nebulizer for patients with respiratory problems. (NIH Photo #1177)

#

Photo Feature

"SMART SPHERE" TECHNIQUE MAY HELP COMBAT DISEASE

A new method of studying cell membranes may eventually lead to a new approach to combating cancer, according to scientists at the California Institute of Technology (Caltech) and its Jet Propulsion Laboratory (JPL).

The work, supported in part by the National Institute of General Medical Sciences, involves the use of microscopic latex spheres whose surfaces are coated with antibodies that instruct them to seek out and attach to specific cells, such as embryonic and tumor cells.

The latex spheres are called "smart" because their antibody coating

(more)

The idea for this "smart sphere" technique was conceived by (clockwise from top, left) Dr. Rembaum; William J. Dreyer, Ph.D., Caltech professor of biology; Robert Molday, Ph.D., Caltech research fellow in biology; and Ms. S. P. S. Yen, senior scientist at JPL (center). Here, they are shown at the console of a scanning electron microscope. (NIH Photo #1178)

"Smart Sphere" (Cont'd)

gives them specificity. Alan Rembaum, Ph.D., of Caltech and JPL, hopes that the spheres can be developed into highly-discriminating vehicles that can carry lethal drugs or radioactive elements to attack cancer or other unwanted cells.

At present the "smart" latex particles are being used in the laboratory to map minute structures on the surfaces of red blood cell membranes. The particles carry dyes and radioactive tracers to mark the submicroscopic structures. This study of the specificity of cell surfaces partly involves the detection and localization of antigens and other receptor molecules on the surfaces of normal, abnormal, and embryonic cells.

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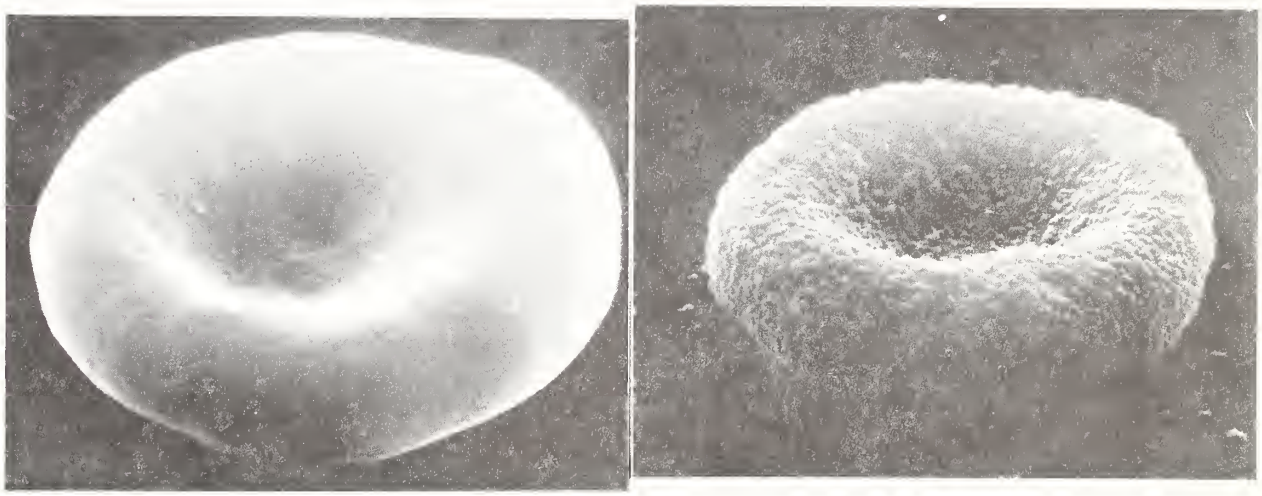
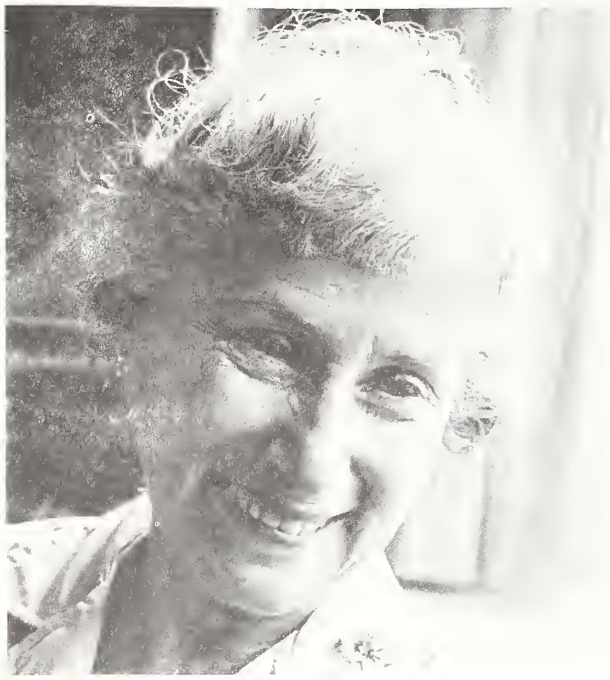


Caltech-JPL scientists placed these red blood cells in a solution containing microscopic latex spheres that had been coated with antibodies. The spheres ignored the cell at left, but latched onto the cell at right which has been coated previously with antigen "locks" that fit the antibody "keys" carried by the spheres. The scientists are investigating the possibility of using this "smart sphere" technique to combat diseases. The scanning electron micrographs are magnified 50,000 times. (NIH Photos #1179, 1180)

Medical News Tip

HUNTINGTON'S DISEASE--An inherited disorder of the nervous system, Huntington's disease (HD), affects men and women alike. It occurs most often in middle life and is usually fatal within five to 15 years of onset.

HD symptoms relate to brain damage, either in the areas for control of muscle movements (such as jerking or twisting), or in the areas for thinking (causing personality changes), or in both.



Marjorie M. Guthrie, widow of folk singer Woody Guthrie who died in 1967 from Huntington's disease. (NIH Photo #1181)

Marjorie M. Guthrie, founder of the Committee to Combat Huntington's Disease, has been named to a four-year term on the Advisory Council of the National Institute of General Medical Sciences (NIGMS).

Mrs. Guthrie's knowledge and perspective of the overall genetic disease problem are assets in her advisory position with NIGMS, which has the primary responsibility to conduct and support research on all forms of hereditary disorders.

The 12-member Advisory Council meets periodically to assess the social and scientific merits of requests by scientists for medical research support, also to monitor progress of the NIGMS programs and formulate policies for their conduct.

For additional information, contact: NIGMS Information Office, Building 31, Room 4A-46, Bethesda, MD 20014, Phone (301 496-5676).

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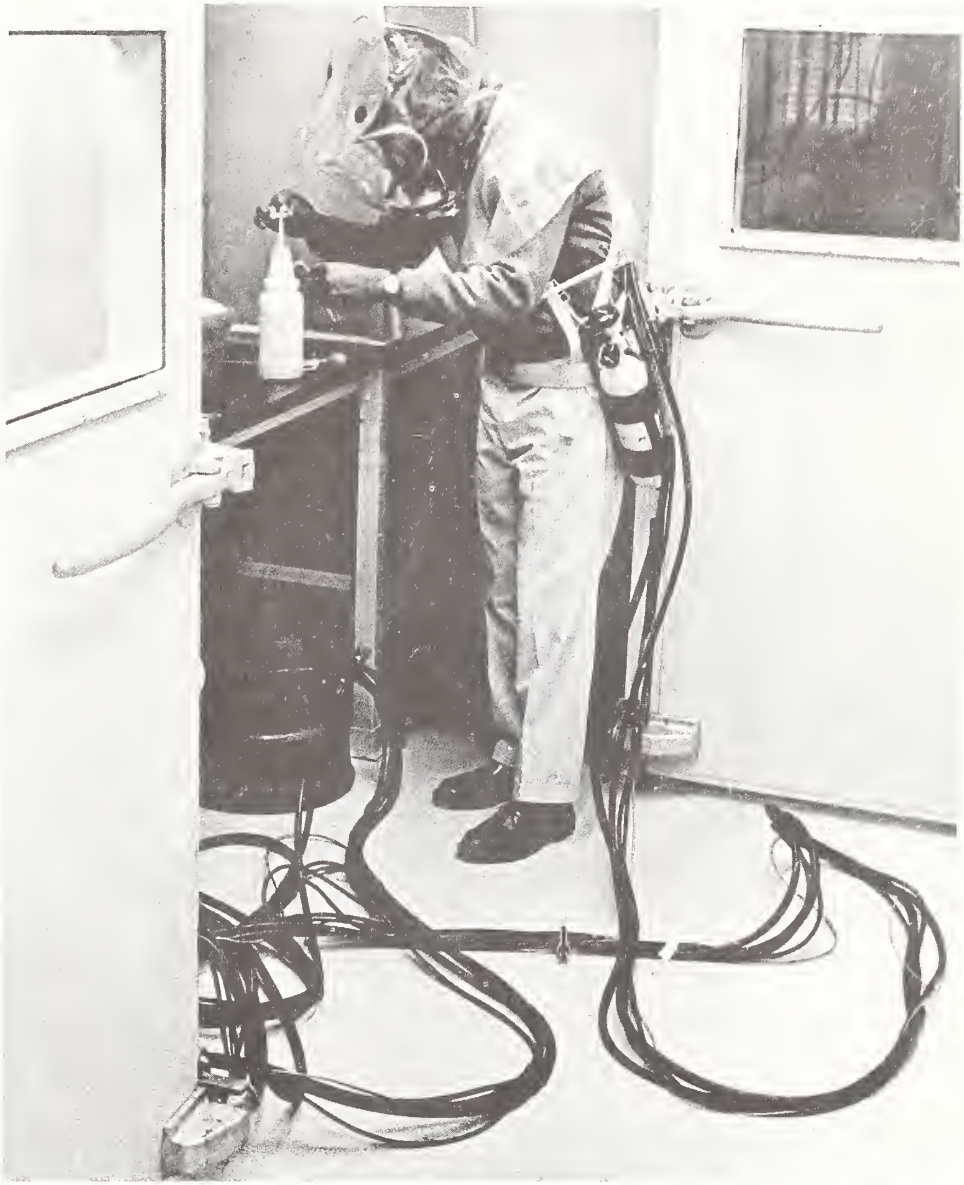
Capsules

RESEARCH ILLUSTRATED



Scientists study the oxygen-free metabolism of cells in the National Heart and Lung Institute anaerobic laboratory. This scientist wears a specially-designed helmet connected to tubes and cables which bring him air to breathe, and vacuum to carry away expired air. The helmet also contains necessary equipment for two-way communication with operators outside the sealed chamber, and an alarm buzzer. The bottle at his left hip contains a back-up supply of compressed air for use in case of emergency. Other safety features have been built into the chamber. (NIH Photo # 1182)

#

New Publication:
The Dust Inhalation Diseases: Pneumoconioses

The National Heart and Lung Institute (NHLI) has released a new publication, *The Dust Inhalation Diseases: Pneumoconioses*, describing occupational lung diseases caused by the inhalation of certain types of dust particles.

One of the most serious of the pneumoconioses is caused by asbestos. Inhaled asbestos fibers cause asbestosis, the crippling disease which scars the lungs and interferes with the passage of oxygen into the blood.

Silicosis, one of the first of the pneumoconioses to be recognized, is caused by breathing silica dust while mining for gold, copper, lead, zinc, iron, or coal.

Black lung disease, officially called Coal Worker's Pneumoconiosis, occurs in an estimated 10 to 20 percent of persons employed in coal mining in the United States.

The new publication discusses these and other dust diseases which present occupational hazards. Causes, symptoms, methods of diagnosis, treatment, and prevention are outlined.

Science writers can obtain a free copy of this publication from:

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